San Francisco VA Medical Center
Grand Rounds

Andrew B. Mick, OD, FAAO
San Francisco VA Medical Center
UC Berkeley School of Optometry
UCSF Department of Ophthalmology

Case Presentation:
- 67 year-old Caucasian male
- Complaint of hazy vision in the right eye
- Gradually worsening for three months
- No difference in blur with or without his glasses

Ocular History:
- S/P LASIK OU
- S/P uncomplicated CEIOL OD six years prior
- S/P uncomplicated CEIOL OS eleven years prior
- Refractive error, presbyopia

Late-postoperative capsular block syndrome

San Francisco VA Medical Center
Grand Rounds

San Francisco VA Eye Clinic:
- Provides eye care to all veterans along coast from San Francisco to Oregon
- Last year, responsible for ~16,000 patient care visits
- Cornea, cataract, vitreoretinal, and oculoplastics surgeries (20-30 / week)
- Prosthetic eyes made on site
- On day when all clinics running ~150-200 patients a day
- Referral center for sub-specialty consultation and surgery for California / Nevada
- Training site for UC Berkeley Optometry and UCSF Ophthalmology

Eye Clinic Staff:
- 6 ophthalmic technicians
- 1 optician
- 1 ocularist
- 5 nurses
- 3 optometrists
- 3 optometry residents
- 2 optometry students
- 3 ophthalmology residents
- 8 subspecialty ophthalmologists
- 1 medical student
- 1 surgical intern

San Francisco VA Eye Clinic Faculty:
- Ayman Naseri, MD: Uveitis Specialist / Cataract Surgeon
- Julie Schallhorn, MD: Corneal and Uveitis Specialist
- Dan Schwartz, MD: Retinal Specialist
- Melissa Luo, MD: Retinal Specialist
- Ying He, MD, PhD: Oculoplastics Specialist
- Joey Hsi, MD: Ophthalmology
- Bryan Winn, MD: Oculoplastics Specialist
- Michele Bloomer, MD: Ocular Pathologist / Cataract Surgeon
- Three optometrists: 60+ years of combined experience

UCSF Medical Center
San Francisco, CA 94143-0996
#16 in Adult Ophthalmology Hospitals
Capsular block syndrome

Examination findings:
• Vision: 20/30 OD 20/20 OS
• Pupils: No APD OU
• IOP: 15/14

Slit lamp examination:
- Lid/lashes: Mild blepharitis
- Conjunctiva: Clear
- Anterior chamber: Deep and quiet
- IOL: Flat, even

Diagnosis:
• Late/postoperative capsular block syndrome

What is it:
• Rare complication of cataract surgery utilizing continuous curvilinear capsulorhexis and posterior chamber in-the-bag intraocular lens implantation

Also known as:
• Capsular bag distension syndrome
• Liquefied afterecataract
• Capsulorhexis-related lacteocrumena

Signs/Symptoms:
- Reduced vision
- Refractive error shift
- Hyperopic: Concave lens effect from fluid build-up
- Myopic: Anterior lens displacement

Timing:
• Average: 3.8 years after surgery
• Range: 2 months to 20 years
• In this case: 6 years
Capsular block syndrome

Differential diagnoses:
- Delayed onset endophthalmitis
- Phacoantigenic uveitis

Capsular block syndrome

Lens Capsule:
- Elastic transparent basement membrane
- Primarily collagen
- Envelops lens
- Zonular insertion sight
- Prevents entrance of large molecules
- Anterior capsule thickens with age
- Produced by the anterior lens epithelium
- Posterior capsule relatively stable thickness throughout life

Capsular block syndrome

Intracapsular cataract extraction (ICCE)
- Removal of the lens and capsule

Conventional extracapsular cataract extraction (ECCE)
- Removal of lens in one piece
- Capsule spared

ECCE by phacoemulsification:
- Fragmentation of lens via ultrasound energy
- Lens removed via aspiration
- Capsule spared

Requires capsulorhexis

Capsular block syndrome

Historical perspective:

- Intracapsular cataract extraction (ICCE)
  - Removal of the lens and capsule
- Conventional extracapsular cataract extraction (ECCE)
  - Removal of lens in one piece
  - Capsule spared
- ECCE by phacoemulsification:
  - Fragmentation of lens via ultrasound energy
  - Lens removed via aspiration
  - Capsule spared

Capsular block syndrome

Anterior capsulotomy:
- Creation of an opening in the anterior capsule
- Lens removed through the created opening
- Posterior capsule left intact

Technique evolution:
- Vogt's Technique
- Kelman's Christmas Tree
- Can Opener
- Envelope
- Continuous Curvilinear Capsulorhexis (CCC)
  - Cystitome
  - Femtosecond Laser-assisted

Capsular block syndrome

Fibrosis:
- Fibrosis of the anterior capsule remnants fuses the edge of the anterior capsule to the anterior surface of the IOL
- Lens removed through the created opening
- Posterior capsule left intact

Closed Chamber:
- Full 360° adhesion between the anterior capsule edges and IOL surface creates a closed chamber between the IOL and the posterior capsule

Fluid Build-Up:
- Turbid fluid accumulates posterior to the IOL

Capsular block syndrome

Pathophysiology

Fibrosis:
- Fibrosis of the anterior capsule remnants fuses the edge of the anterior capsule to the anterior surface of the IOL
- Lens removed through the created opening
- Posterior capsule left intact

Closed Chamber:
- Full 360° adhesion between the anterior capsule edges and IOL surface creates a closed chamber between the IOL and the posterior capsule

Fluid Build-Up:
- Turbid fluid accumulates posterior to the IOL

Pathophysiology

Lens epithelial cell proliferation
- Production of collagen and extracellular matrix
- Release proinflammatory cytokines
- Increased osmolarity within capsule
- Promote capsule fibrosis
- Water drawn into capsule
Capsular block syndrome

What is in the bag?

- Lens epithelial cell proliferation?
- α-crystallin
- β-crystallin
- Inflammatory response?
- TNF-α
- IL-1β
- Infectious agent?
- Propionibacterium acne

Incidence and Risk Factors

- Incidence: 0.27% over 37 months
- IOL properties:
  - Haptic design
  - Angulation
  - Material
  - Axial length > 25 mm

Incidence and Risk Factors

- Nd:YAG laser capsulotomy
- Anterior or posterior capsule
- Surgical management:
  - Posterior continuous curvilinear capsulorhexis (PCCC)
  - Anterior capsule release, fluid aspiration, and irrigation of posterior capsule
- Spontaneous resolution
  - Contraction of fibrosis

Treatment

* Nd:YAG laser capsulotomy

Before Laser

After Laser

Anterior chamber OCT

Pre-laser

Post-laser

Vision returned to 20/20
Capsular block syndrome

• Capsular block syndrome can arise months to years after uncomplicated cataract surgery
• Characterized by milky fluid sequestered behind the IOL within the posterior capsule
• Secondary to fibrotic adhesion of the anterior capsule edges to IOL surface after capsulorhexis and in-the-bag PCIOL placement
• Distinguishable from other late complications of cataract surgery by lack of robust concurrent ocular inflammation
• Treatment with laser capsulotomy is typically successful with few complications

Take Home Points:
Andrew B Mick, OD, FAAO
San Francisco VA Medical Center
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Common clinical scenario in practice

54-year-old male comes in for diabetic retinopathy screening examination
Right eye only corrects to 20/25 vision, left eye 20/20
Dilated fundus examination for the right eye shows a mild nonproliferative diabetic retinopathy with a few microaneurysms near the fovea

Role of OCT in Diabetic Macular Edema

ETDRS-based definition
- A clinical diagnosis
- Retinal thickening within 500 um of foveal center

Clinically significant macular edema (CSME):
- Retinal thickening within 500 um of foveal center
- Hard exudates within 500 um of foveal center associated with retinal thickening
- Retinal thickening of 1 disc-diameter in size within 1 disc-diameter of the foveal center

OCT center zone average thickness 284 um
Do you have to refer?
Clinically significant macular edema (CSME):
• A clinical diagnosis
• Hard exudates within 500 μm of foveal center associated with retinal thickening

Role of OCT in Diabetic Macular Edema
ETDRS-based definition

Clinically significant macular edema (CSME):
• A clinical diagnosis
• Retinal thickening of one disc-diameter within one disc-diameter of foveal center

Major Results:
From baseline to one year, the mean visual-acuity letter scores improved:
- Aflibercept: 13.3 letters, p<0.001
- Bevacizumab: 9.7 letters
- Ranibizumab: 11.2 letters

Statistical significance of treatment depended on VA:
- Vision better than 20/50 No difference between drugs
- Vision worse than 20/50 Aflibercept had better outcomes

Protocol T
Defining Center Involving Macular Edema
Protocol T inclusion criteria:
- Diabetic macular edema affecting the central macula
- Vision 20/30 or worse
- OCT center zone thickness more than threshold for device

OCT center zone thickness thresholds:
- Zeiss Status®: >250 μm (Time Domain)
- Zeiss Cirrus®: >305 μm for men / >290 μm for women
- Heidelberg Spectralis®: >320 μm for men / >305 for women

Methods:
- 702 Type I and II diabetics with center involving diabetic macular edema
- Vision 20/25 or better
- Randomized to intravitreal aflibercept, focal/grid laser, or observation
- Aflibercept treatment started in laser and observation group if vision dropped by at least 10 letters (~more than 2 lines) at any visit or 5-9 letters (1-2 lines) on 2 consecutive visits

At two years, the percentage of eyes with a 5-letter decrease in VA:
- Aflibercept: 16%
- Laser: 17%
- Observation: 19% p = 0.79

Conclusions:
Among eyes with center involving diabetic macular edema and good vision, there was no significant difference in vision loss after 2 years, whether eyes were initially managed with aflibercept or with laser or observation and given aflibercept if vision worsened
Do you have to refer for this clinical scenario?

**Vision 20/25:**
- Clinically visible microaneurysms near foveal center
- OCT line scan shows small intraretinal cyst within 500 um infero temporal to fovea
- OCT center zone average thickness 284 um

**Criteria for intervention significant diabetic edema**

Clinically significant macular edema (CSME):
- Retinal thickening within 500 um of foveal center
- Hard exudates within 500 um of foveal center associated with retinal thickening
- Retinal thickening of 1 disc-diameter in size within 1 disc-diameter of the foveal center

Center involving diabetic macular edema:
- Vision 20/30 or worse and significant center involving edema

OCT center zone thickness thresholds:
- Zeiss Status©: > 250 um (Time Domain)
- Zeiss Cirrus©: > 305 um for men / > 290 um for women
- Heidelberg Spectralis©: > 320 um for men / > 305 for women

No OCT

With OCT

**San Francisco VA Medical Center Grand Rounds**

Shifting standards in the management of cranial nerve III, IV, and VI palsy

Andrew B. Mick, OD, FAAO
San Francisco VA Medical Center
UC Berkeley School of Optometry
UCSF Department of Ophthalmology

68 year-old black female

Walk-in for new onset double vision

Examination shows 3+ restriction in abduction in the right eye

Diagnosis: Isolated right cranial nerve six palsy
10/8/19

82 year-old Asian male

Presenting with 1-day history of double vision
Mild exotropia and hypotropia of left eye.
Also noted to have ptosis of the left upper lid
Ocular motility full OD

82 year-old Asian male

Ocular motility OD

2+ restriction in adduction, no restriction in abduction
Cranial nerve VI is intact

In attempted adduction:
• 1+ restriction in elevation
• No restriction in depression
Cranial nerve IV is intact

In abduction:
• 2+ restriction in elevation
• 1+ restriction in depression
Normal pupil functioning

82 year-old Asian male

Diagnosis: Isolated left cranial nerve III palsy
Partial external involving (Extraocular muscle)
Not internal involving (Pupil)

No headache or recent head trauma
Systemic history: Hypertension
Hyperlipidemia

 What is your management?

82 year-old Asian male

The Rule of the Pupil

Diagnosis: Isolated left cranial nerve III palsy
Partial external involving (Extraocular muscle)
Not internal involving (Pupil)

Systemic history: Hypertension
Hyperlipidemia
No headache or recent head trauma
What is your management?

The Rule of the Pupil

Definition:
When a compressive aneurysm, usually of the posterior communicating artery, is
the cause of a CNIII palsy, pupillary function is usually affected

Anatomical Basis:
• Pupil fibers of CNIII lie on the superficial, dorsomedial portion of the nerve in
  the subarachnoid space
• Aneurysms of the posterior communicating artery can compress CNIII in the
  subarachnoid space
• In contrast, ischemia from small vessel disease tends to affect the
  central part of the nerve where the motor fibers lie and therefore
  spares the pupillary fibers

The 82-year-old Asian male was pupil sparing, and he had microvascular risk
factors, can he be monitored without imaging?

The Rule of the Pupil

NOT TO BE FOLLOWED NOW!!!!!!

The Rule of the Pupil

Older individuals (age > 50 years) with acute isolated ocular motor cranial mono-
neuropathy (CN IV and VI) with microvascular risk factors (diabetes, hypertension,
hyperlipidemia, smoking) may be followed without neuroimaging for approximately
three months as spontaneous resolution of microvascular palsies is expected in
about 8-10 weeks.

Pupil-sparing CNIII palsies in older patients with vascular risk factors are presumed
to be microvascular in etiology and can be monitored closely without neuroimaging
for ~ 3 months

The Rule of the Pupil

To apply the rule:
• The CNIII should be neurologically isolated
• The CNIII should be complete externally (both superior and inferior
  branches completely affected)
• The involved eye should be down and out with ptosis
• The patient should have vascular risk factors (hypertension, diabetes)
• The patient should be over age 40

In the previous case, can the “Rule of the Pupil” be applied?

No, it was not a complete external palsy!!!
Risk of aneurysm as cause of CNIII palsy:

- Complete external (EOMs) / Normal internal (Pupil) 3%
- Partial external (EOMs) / Normal internal (Pupil) 33%

The Rule of the Pupil


Why the “Rule of the Pupil” should not be used in acute CNIII palsies

- A normal pupil reduces the chance there is an aneurysm, it doesn’t eliminate it
- Aneurysm in other locations (ex: basilar tip) can compress the CNIII and not affect the pupil fibers
- The pupil can become involved days to weeks after an initially normal examination
- When the Rule of the Pupil was devised, imaging was done with catheter angiography (risk of mortality and morbidity) and prior to widespread availability of advanced imaging techniques
- MRI/MRA and CT/CTA are now available with dramatically reduced risk of mortality and morbidity
- Missing an aneurysm carries a significant risk of morbidity
- Average time from the onset of CNIII palsy from aneurysm to rupture is 29 days
- Mortality rate of 50% in ruptured aneurysm

Scan all CNIII palsies IMMEDIATELY regardless of pupil function!!


Patients, over the age of 50, with isolated CNIII, CNIV, and CNVI palsies within 30 days of onset

Group 1:
- Non-vasculoplastic risk factors:
  - eye pain
  - headache
  - progressive diplopia
  - cancer history
  - history of immunosuppression

Group 2:
- Vasculopathic risk factors

MRI of the brain with and without gadolinium was obtained for all subjects


Group 1: 34.4% had non-vascular causes of the cranial nerve palsy:
- Neoplasms
- Pituitary apoplexy
- Pachymeningitis
- Herpes zoster

Group 2: 10% had non-vascular causes of cranial nerve palsy:
- Giant cell arteritis
- Neoplasm
- Midbrain infarction
- Pituitary apoplexy

Subgroup of Group 2, excluding CNIII palsies

In this special subgroup, 4.7% of the CN IV and CN VI palsies had a causative lesion detected on MRI

Authors’ Conclusions:

“Given the higher incidence of other causes found in our cohort of patients, early neuroimaging is recommended as a general guideline in all patients presenting with acute isolated ocular motor palsies, especially when the patient presents to a non-specialist.”

Should we be immediately scanning all acute CN VI and IV palsies like we do for CNIII palsies?

68 year-old black female with CN VI palsy

Seen one month later with only a mild restriction in abduction in the right eye.

At two months, extracocular motility was normal

Diagnosis: Resolved microvascular isolated right cranial nerve six palsy

82 year-old Asian male with CNIII palsy

Urgent referral to ER

Urgent referral to ER

To Review

This is the management of ALL acute CNIII palsies

San Francisco VA Medical Center Grand Rounds

All acute CNIII palsies require IMMEDIATE MRI/MRA or CT/CTA regardless of pupil functioning

Acute CNIV and CNVI palsies need immediate neuroimaging and workup if:
- Patient is under age 50
- Patient does not have vasculopathic risk factors
- Patient has a history of cancer
- Patient could have giant cell arteritis as a possible cause
- Cranial nerve palsy is not isolated or there other neurologic signs

All presumed vasculopathic CNIV and CNVI palsies can be followed monthly, but worked-up if not resolved at 3 months

There is growing opinion that even CNIV and CNVI palsies should be worked-up immediately

San Francisco VA Medical Center Grand Rounds

Prescribing antibiotics to patients who are on warfarin

Andrew B Mick, OD, FAAO
San Francisco VA Medical Center
UC Berkeley School of Optometry
UCSF Department of Ophthalmology
67 year old caucasian male 1-day post-op left lateral lid cyst removal

Examination note mentions small internal hordeolum medial upper eyelid same day as surgery that was internally expressed at time of lid cyst removal

Carries diagnosis of atrial fibrillation

Current warfarin dose:
• 4.0 mg Monday, Tuesday, Wednesday, Friday, Saturday
• 3.0 mg Thursday, Sunday
• Most recent INR: 2.4

Concern for preseptal cellulitis? Who would Rx an oral antibiotic?

You have patients like this in your practice!!

Atrial fibrillation:
• The most common sustained cardiac arrhythmia
• Affects 1-2% of the general population
• Affects 5% of individuals over the age of 65 in the United States

Patients with atrial fibrillation are at high risk of stroke:
• Having AF confers a 5x increased risk of stroke
• Atrial fibrillation responsible for one in five strokes
• Stroke occurs in 23.5% of patients aged 80-90 years with A fib

You have patients like this in your practice!!

Atrial fibrillation:
• The most common sustained cardiac arrhythmia
• Affects 1-2% of the general population
• Affects 5% of individuals over the age of 65 in the United States

Mechanism of action:
• Inhibition of the synthesis of vitamin K dependent clotting factors
• Factors II, VII, IX, and X
• Protein C and S

Warfarin reaches peak serum concentrations within 4 hours

Warfarin is almost completely metabolized by hepatic cytochrome P-450 with effective half life ranging from 20-60 hours

Inactive metabolites are excreted by the kidneys in the urine for about a week

Indication for use:
• Atrial fibrillation
• Thromboembolism prophylaxis after heart valve replacement
• Thromboembolism prophylaxis after myocardial infarction
• Venous thromboembolism prophylaxis

Reduces the risk of systemic thromboembolism including stroke from 60-84% in patients with atrial fibrillation

Reduces the rate of stroke by 50% after myocardial infarction and the rate of recurrent myocardial infarction by 35%

Reduces the risk of systemic thromboembolism and bleeding complications by 60-90% in patients with mechanical heart valves

1.3% of warfarin patients have major bleeding events within 30 days of initiation

Major bleeding events within 30 days of warfarin initiation:
• Intracranial hemorrhage 9%
• Gastrointestinal tract bleed 22%
• Gross hematuria 4%
• Gluteal/high hematoma 4%
• Retroperitoneal 1%
• Pulmonary hemorrhage 1%

Co-administration of antibiotics can potentiate effects of warfarin

Inhibitors of cytochrome P-450 isoenzymes have the potential to increase warfarin anticoagulation effects

Shireman. Chest 2006;130:1390-6

100 patients with history of ischemic stroke treated with warfarin:
• Major bleeding events occurred in 14% at one year
• Major bleeding events occurred in 26% at five years


Oral Antivirals (acyclovir, valacyclovir, famciclovir)
• Oral Antibiotics

Oral Antivirals (acyclovir, valacyclovir, famciclovir)

Oral Antibiotics
A total of 22,272 patients

Antibiotics considered to be high risk for interaction with warfarin include: trimethoprim/sulfamethoxazole (TMP/SMX®, Bactrim®), ciprofloxacin, levofloxacin, metronidazole, fluconazole, azithromycin, and clarithromycin.

Low-risk antibiotics include clindamycin and cephalexin.

High-risk antibiotics were associated with increased risk of bleeding as a primary diagnosis. TMP/SMX®, ciprofloxacin, levofloxacin, azithromycin, and clarithromycin were associated with serious bleeding as a primary or secondary diagnosis.

Mean change in INR by antibiotic:
- Azithromycin 0.51
- Levofloxacin 0.85
- TMP/SMX (Bactrim®) 1.7%

Incidence of supratherapeutic INR by antibiotic:
- Azithromycin 31%
- Levofloxacin 33%
- TMP/SMX (Bactrim®) 69%

International Normalized Ratio:
- The PT on a normal individual varies because of the different batches of tissue factor used in the test
- Manufacturers must assign an International Sensitivity Index (ISI) for any tissue factor they manufacture so an INR can be calculated to standardize the results
- Reference range: 0.8 – 1.2

Prothrombin Time:
- Used to determine the clotting tendency of the blood
- Assay evaluating the extrinsic pathway of coagulation
- Time in seconds for prepared sample to clot after addition of tissue factor
- Reference range: 11-14 seconds

Warfarin therapy monitored by PT and INR:

PT and INR in our patient treated with Keflex
- Prothrombin Time:
  - Two months before cephalexin: 26.5 seconds
  - One month before cephalexin: 26.6 seconds
  - 48 hours on cephalexin: 26.9 seconds
- International Normalized Ratio (INR):
  - Two months before cephalexin: 2.3
  - One month before cephalexin: 2.3
  - 48 hours on cephalexin: 2.4

Other anticoagulants on the market

Came to market in last ~3 years

Factor Xa Inhibitors:
- Apixaban (Eliquis®) Oral tablets
- Fondaparinux (Arixtra®) Injections
- Rivaroxaban (Xarelto®) Oral tablets
- Edoxaban (Savaysa®) Oral tablets

Less likely to have adverse interactions with antibiotics
Bilateral simultaneous angle closure with a posterior cause!

48 year-old Caucasian female

Walk-in for bilateral eye redness

Seen in the emergency room six days earlier, diagnosed with viral conjunctivitis and sent home

Presented to the SFVA Eye Clinic for a second opinion, concerned it may be related to a newly prescribed medication

48 year-old Caucasian female

Visual acuities:
- OD: 20/60, pinhole 20/40
- OS: 20/60, pinhole 20/40

Intraocular pressures:
- 12 mmHg by Goldmann Tonometry

Pupils:
- Irregular pupil shape OD
- No afferent pupillary defect OU

Slit lamp examination:
- Anterior chambers were noted to be extremely narrow OU
- 4+ conjunctival hyperemia OU
- 2+ anterior chamber reaction OU
- Posterior synechiae 6:00 – 10:00 OD (distorting the pupil)

UBM Images: 360 degree ciliochoroidal effusions OU

Summary of examination findings

Clinical Findings:
- Bilateral ciliochoroidal effusions
- Bilateral secondary closure of the irido-corneal angle
- Anterior uveitis

History:
- No evidence of nanophthalmia
- Not a high hyperope
- No recent surgery or laser procedures on the eye

What was the new medication you started?

“Topiramate”
**Targeted medication history**

- Started topiramate for chronic migraine headaches 12 days prior.
- Initial dose was 12.5 mg b.i.d. x 2 weeks.
- Planned increase in therapy to 25 mg b.i.d. thereafter.
- Had used for 6 days before self-discontinuing on the day she presented to the ER (6 days before presenting to eye clinic).

**Diagnosis:**
- Topiramate induced ciliochoroidal effusion
- Bilateral secondary angle closure

**Treatment:**
- Cyclopentolate 1% bid
- Prednisolone acetate 1% qid

**Nine day follow-up**

- Patient again reported improved symptoms and vision.
- Conjunctival injection almost completely resolved.
- Vision:
  - 20/20 OD
  - 20/20 OS
- Anterior chamber cell down to 1+ OD and trace OS.
- IOP: 14/11
- UBM: Showed the following.

**UBM Images: Resolution of ciliochoroidal effusions OU**

- Initial presentation: six days after discontinuing topiramate.
- 15 days after discontinuing topiramate and 8 days of topical steroid / cycloplegic.

**UBM Images: Resolution of ciliochoroidal effusions OU**

**Natural history and typical presentation**

- Based on 100+ reported cases of topiramate induced angle closure.
- Laterality: 97% bilateral.
- Age at time of diagnosis: 34-39 years (Range 3-70).
- Sex: Women > Men.
- Topiramate start—presentation: 7-12 days (Range 1-49).
- Dosage of topiramate: 53 mg/day (Range 25-150).
- Associated signs: Anterior uveitis.
- Average IOP at diagnosis: 47 mmHg.
- Typical time to resolution: 3 days – 6 months.

**Other ophthalmologic sequelae of topiramate**

- Seen in our patient and typical:
  - Ciliochoroidal effusion
  - Secondary angle closure
  - Myopic shift
  - Nongranulomatous anterior uveitis

- Non seen in our patient and rare:
  - Vitritis
  - Transient retinal striae
  - Transient RNFL thickening

**Topiramate Review**

- Sulfa-derivative monosaccharide.
- Sold under the trade names: Topamax®(Janssen Pharmaceuticals, Belgium)
  - Trokendi XR® (Supernus Pharmaceuticals, Rockville, MD).
- Over 32 million prescriptions have been written for topiramate.

**Targets of action:**
- Voltage gated sodium channels
- High-voltage activated calcium channels
- Postsynaptic GABA receptor activity
- AMP/kainate receptors
- Inhibition of some carbonic anhydrase isoenzymes.
Topiramate Review

Original FDA approval in 1996 to treat epilepsy and in 2004 for migraine prophylaxis.

In last decade numerous uses have been suggested in the literature:
- Bipolar disorder
- Alcohol dependence
- PTSD
- Obesity
- Eating disorders
- Tobacco dependence
- Essential tremor
- Tourette’s disorder
- Postherpetic neuralgia

51-year old man who developed bilateral angle closure intraocular pressure was 32 OD and 58 OS

Occurred 2 weeks after beginning topiramate

Mechanism of topiramate induced angle closure:
- Induction of ciliochoroidal effusions
- Ciliary body edema and anterior rotation of the ciliary body
- Forward displacement of the lens-iris diaphragm
- Swollen ciliary body results in relaxation of zonular traction causing anterior – posterior lens thickening

Idiosyncratic drug reactions:
- Adverse drug reactions that do not occur in the vast majority of patients taking a drug
- Do not involve the therapeutic effect of the drug
- Tends to be unpredictable (dose independent) and can be life-threatening
- Have an immune basis

Sulfonamide induced idiosyncratic reactions:
- Sulfonamides metabolized in the liver
- A small quantity of nonreactive metabolites bind to protein and are stable enough to circulate from the liver to remote tissues
- The local tissue specific metabolic environment leads to the creation of reactive metabolites that illicit an immune response
- Genetic factors and disease states may play a role in which individuals will have an immune response to these local metabolites

Topiramate induced angle closure treatment:
- Discontinuation of topiramate
- Cycloplegics (Retraction of the ciliary processes)
- Systemic steroids
- Hyperosmotics
- Avoid oral acetazolamide / pilocarpine

Controlling intraocular pressure:
- Topical beta-blockers, alpha-agonists
- Hyperosmotics
- Avoid oral acetazolamide / pilocarpine

Role of laser iridotomy is controversial:
- Not a pupillary block mechanism
- Despite this, ~25% of the cases in the literature used LPI
Although ocular side effects are rare, the indications for topiramate have dramatically increased in the past decade. Consider topiramate (or other sulfonamide derivatives) as a cause of angle closure in atypical populations and presentations. Vast majority of cases resolve with discontinuation of topiramate along with topical glaucoma drops, cycloplegics and topical steroids. Even with appropriate therapy, associated inflammation can take months to resolve.

Andrew B. Mick, OD, FAAO
San Francisco VA Medical Center
UC Berkeley School of Optometry
UCSF Department of Ophthalmology

61 year old Caucasian male
Asymptomatic
Glaucoma suspect follow-up
Ocular History:
- Glaucoma suspect based on nerve appearance
- Last dilated 5 years prior
Medical History:
- Hyperlipidemia
- PTSD
- Colon Polyps
- Tobacco / Marijuana dependence

Fundus examination

Whitish lesion in superior temporal arcade, overlying retinal detachment

SD-OCT Showing Extent of Retinal Elevation

Yellow-white lesion itself was not elevated
Caliper measurement shows overlying RD ~ 1200 um
Differential Diagnosis?

- Amelanotic choroidal nevus/melanoma
- Choroidal metastasis
- Intraocular lymphoma
- Sclerochoroidal calcification
- Choroidal Osteoma

Concerning given his smoking history and associated RD
Less likely to be sharply demarcated. No CNS lymphoma diagnosis and no vitritis

Les sharply demarcated. Often show lesion elevation

Osteoma vs. Sclerochoroidal Calcification

- Younger ages (20 – 30 years)
- Female predilection
- Mostly white but also in black and Asian populations
- Most common near disc
- 80% unilateral
- RPE clumping and thinning on surface
- Vascular “spiders” on surface
- 1/3 will eventually develop CNVM

- Older ages (median ~ 70 years)
- No sexual predilection
- Almost exclusively in whites
- Superior and inferior arcades
- 40-50% bilateral
- Often an overlying RD

Key Diagnostic Test: Ultrasonography

B-scan ultrasonography showing acoustic hyper reflectivity

Based on the B-scan ultrasonography:
- Sclerochoroidal calcification or choroidal osteoma

Osteoma vs. Sclerochoroidal Calcification

Dystrophic:
- Areas of tissue damage or necrosis
- People have normal calcium and phosphorus levels
In the eye:
- Band keratopathy
- Senile scleral plaques
- Optic disc drusen
- Sclerochoroidal calcification

Metastatic:
- Deposits of calcium salts in normal tissues as a result of alterations in calcium and phosphorus metabolism
In the eye:
- Sclerochoroidal calcification

Sclerochoroidal Calcification: Systemic Associations

Disorders of calcium/phosphorus metabolism:

Hyperparathyroidism:
- Primary hyperparathyroidism: Tumor or idiopathic hyperplasia
- Secondary hyperparathyroidism: Diffuse hyperplasia of all glands

Pseudohyperparathyroidism:
- Hereditary condition: Round face, stocky build, short stature

Hyperparathyroidism:
- Results in hypercalcemia through excess GI tract calcium absorption

Most in VA population are idiopathic
Calcium/Phosphorus labs ordered:

- Parathyroid Hormone 35.2 \( \text{pg/ml} \)
- Serum phosphorus 2.5 \( \text{mg/dl} \)
- Serum Calcium 9.1 \( \text{mg/dl} \)

RTC 6 months for routine follow-up.

Sclerochoroidal Calcification Clinical Features:

Earliest calcification occurs in the sclera, then the choroid, then disruptions / atrophy of the overlying RPE.

Occasionally can be seen externally prior to choroidal involvement.

Sclerochoroidal Calcification Clinical Features:

Yellowish, white round lesions in superior or inferior arcades.

Some lesions have yellow halos around perimeter of lesion.

Sclerochoroidal Calcification Clinical Features:

Varying amount of RPE atrophy / disruption within or around the lesions.

Sclerochoroidal Calcification Clinical Features:

50% are multifocal.

Bilateral in 40 – 50% of cases.

Overlying serous retinal detachment not uncommon.

Choroidal neovascularization has been reported.
Sclerochoroidal Calcification: Back to our patient

Work-up / refer unless classic presentation:
- Older aged Caucasian patients (> 65 years)
- Lesions in arcades
- Hyper-reflective with B-scan
- Contact PCP for labs testing calcium phosphorus metabolism especially in atypical groups

Andrew B. Mick, OD, FAAO
San Francisco VA Medical Center
UC Berkeley School of Optometry
UCSF Department of Ophthalmology