Michael S. Lee · Kathleen B. Digre

A Case-Based Guide to Eye Pain

Perspectives from Ophthalmology and Neurology



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Foreword

"I have pain in (or around or behind) my eye." This sentence is one that most physicians, be they ophthalmologists, optometrists, neurologists, or primary care providers, dread to hear. In large part, this is because pain is such a subjective complaint. Thus, the first assumption that most physicians make when they see a patient with the complaint of "eye pain" is that they will not find the cause of the pain. This, in turn, will make them believe that it is most likely that (1) there is nothing really wrong with the patient, (2) the patient will be unhappy with them, and (3) the patient will want some type of drug for the pain.

In reality, pain is a complex symptom with many etiologies. On the one hand, its cause may be something straightforward, like a dry eye, and its treatment may be as simple as ocular lubrication or punctal occlusion. On the other hand, patients with eye pain may have a potentially vision-threatening condition such as intermittent angle-closure glaucoma or even a life-threatening condition such as an intracranial aneurysm or tumor. The ophthalmologist who finds no ocular cause for the patient's complaints is sure to be perplexed as will the neurologist who finds no neurologic cause and who obtains neuroimaging that is unremarkable. The primary care provider may not even know to whom to refer the patient or what to do when the patient returns from the general ophthalmologist and/or neurologist with no diagnosis. Even neuro-ophthalmologists are not immune to the confusion that comes in dealing with patients who have eye pain. A Case-Based Guide to Eye Pain—Perspectives from Ophthalmology and Neurology, written by two neuro-ophthalmologists, Dr. Mike S. Lee, an ophthalmologist, and Dr. Kathleen B. Digre, a neurologist, thus is a welcome addition to everyone's practice, particularly as it is, as the title indicates, case based—like a conversation with a colleague.

The book begins with a chapter on key signs and symptoms, emphasizing their importance in diagnosis. There follows a list of the various abbreviations used in the book. The subsequent cases, all of which contain excellent figures and illustrations, are then grouped into two main sections. The first section contains 18 cases demonstrating ocular causes of pain, ten with relatively normal examination findings and eight in which there are abnormal but often subtle findings. The second section contains 25 cases demonstrating neurologic causes of eye pain, 15 in patients with

vi Foreword

little or no neurologic or eye findings and ten with abnormal findings. All 43 cases begin with the history and examination, followed by commentary by both Dr. Lee and Dr. Digre. Thus, the reader gets the views of both an ophthalmologist and a neurologist. Each case ends with a summary, key points, and references for the reader who wishes to pursue the topic further. The book ends with four appendices. Appendix 1 lists the tables in the book. Appendix 2 lists the figures in the book. Appendix 3 discusses how to obtain a proper history and perform an appropriate examination in a patient with eye pain, and Appendix 4 discusses the pathophysiology of eye pain.

Although eye pain is frustrating for patients and can be frustrating for the physicians who care for such patients, the diagnosis and treatment of its cause can not only improve a patient's quality of life but also can prevent major ocular or neurologic morbidity. This book fills a void in the ophthalmic, neurologic, and general medical literature and should be on the shelf in every physician's office.

Neil R. Miller, M.D., F.A.C.S.

Preface

Most of us have a "Do not schedule this with me" diagnosis list, and many of our colleagues have told us that "eye pain" resides near the top of that list. Unfortunately, there is not a good department for these patients, and there are a lot of them showing up in our offices and clinics. In our neurology and ophthalmology residencies and fellowships, we never received formal teaching or training in eye pain and, honestly, had to learn a lot by trial and error (and by fire). So when a Springer editor approached us in the fall of 2015 about writing a book about the subject, it intrigued us.

She told us that no book on eye pain existed and that readers enjoy case-based books. So, we set out to demystify the topic and create a practical approach to the patient with eye pain. At first, we thought to target neurologists and ophthalmologists, but, as we inquired around, our colleagues in the emergency room and urgency room and primary care asked if they could read some of the chapters as well.

There are 43 cases but more than 43 causes of eye pain. We use each case as a springboard to generate a differential diagnosis and a thought process based on the signs and symptoms. Some of the cases are not classic, but most of our patients don't always follow the book.

We have tried to give the International Classification of Headache Disorders whenever possible. For a complete listing of these disorders please see: International Headache Society Headache classification ICHD 3 beta. Cephalalgia 2013; 33(9):629–808.

We sincerely hope that you will enjoy this book and, after reading it, feel more comfortable serving our patients with eye pain.

Minneapolis, MN Salt Lake City, UT Michael S. Lee Kathleen B. Digre

Acknowledgements

I would like to thank my loving wife, Mina, and my children, Sam, Nate, Isaac, and Esthergrace, who mean the world to me. Your faith and your support make all the difference and you are truly a gift and a blessing from above. Thanks to Yong and Soo Lee and Hyung and Kilja Kim for your loving support and sacrifice. I would also like to thank Nicholas Volpe, Simmons Lessell, Joe Rizzo, Mike Siatkowski, and Andy Lee who have mentored me along in my career. Greg Kosmorsky has taught me a lot about eye pain and about life in general. Finally, I would like to thank my coauthor, Kathleen, who has made writing my first book an extremely positive experience. It has been a pleasure working with you.

Michael S. Lee, MD

I would like to thank people who have really taught me about eye pain and headache. My mentor, James Corbett, instilled in me an enthusiasm for the study of the eye and headache. I have also learned a lot about eye pain and headache from my wonderful colleagues Susan Baggaley, Judith Warner, Bradley Katz, and Alison Crum at the Moran Eye Center, University of Utah. Finally, I would like to thank my wonderful supportive husband, Michael Varner, and children Johanna and Gita Varner for their encouragement. Thanks to you Mike for a wonderful, educational experience writing this book—it has been fun.

Kathleen B. Digre, MD

We both would like to thank our patients who teach us about eye pain in all of its varied forms and keep us wanting to learn more.

Supported in part by an Unrestricted Grant from Research to Prevent Blindness, Inc., New York, NY, to the Department of Ophthalmology & Visual Sciences, University of Utah.

Signs and Symptoms

Dyspersorment of comment evolutions (X)	Case	Diagnosis	VA lose*	Red	White	Procie	Eyelid	Anicocoria	Prontocie	Tearing	Nasal	Dinlonia	Blurry	Other Photonhohia comment	Other
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(X) (X) (X) (X) (X)		Orbital mass	(X)	\otimes	(X)	(X)	8		×	(X)		(X)	(X)	(X)	
		Ocular ischemic syndrome	$\widehat{\mathbb{X}}$	8	8			(X)					(X)	(X)	TVL in light

(continued)

Case	Diagnosis	VA loss*	Red	White	Ptosis	Eyelid edema	Anisocoria	Proptosis	Tearing	Nasal sxs	Diplopia	Blurry vision	Blurry Other vision Photophobia comment	Other
17	Horner syndrome		8	\mathbb{X}	×		×		(X)	8				+/- anhidrosis
18	Microvascular cranial nerve palsy			×	(X)		(X)				×			Ptosis and anisocoria w/3np only
19	Migraine			×									×	Aura may cause TVL
20	Medication overuse headache			×										
21	Photophobia		\propto	(X)									X	
22	Trigeminal neuralgia			×										
23	Cervicogenic headache			×									(X)	
24	Ice pick headache			×										
25	Sinus disease			X						X				
26	Tension type headache			×									(X)	
27	Supraorbital neuralgia			×									(X)	
28	Trigeminal autonomic cephalalgia		×		X		X		X	×			X unilat	
29	Cough headache			×										
30	Traumatic headache			×									X	
31	Intracranial hypotension			×							(X)		(X)	Positional pain
32	Giant cell arteritis	(X)	(X	(X)	(X)	(X)	(X)				(X)	(X)		>50 yo

33	Thunderclap headache			×							8	(X)	
34	Meningitis	(X)	(X)	(X)						(X)	8	X	
35	Optic neuritis	×		×							×		
36	Idiopathic intracranial hypertension	8		×						8	8	(X)	
37	Carotid cavernous fistula	8	×		(X)	(X)	(x)	8		(X)	8	(X)	
38	Herpes zoster ophthalmicus	8	<u>&</u>	8	(X)	×		<u>(X)</u>		(X)	8	(X)	Pain may antedate vesicles
39	Periocular skin cancer	(X)		×	(X)		(X)	(X)		(X)	<u>X</u>		
40	Tolosa Hunt		\propto	(X)	(X)	(X)	(X)	(X)	(X)	(X)	8	(X)	
41	Pituitary tumor	(X)		×						(X)	8	(X)	
42	Aneurysm	(X)		X	(X)		(X)			(X)	(X)	(X)	
43	Ophthalmoplegic migraine			×	×		×			×		(X)	<10 yo

X = Commonly occurs (X) = Possibly occurs

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Abbreviations

3NP Third nerve palsy

ABMD Anterior basement membrane dystrophy

ACE Angiotensin-converting enzyme

ANA Antinuclear antibody
APD Afferent pupillary defect

BB Ball bullet BE Both eyes C Cervical

c-ANCA Cytoplasmic antineutrophil cytoplasmic antibodies

C-C Carotid cavernous
CAS Clinical activity score
CBC Complete blood count
CI Convergence insufficiency

CISS Constructive interference in steady state

cm Centimeter(s) CN Cranial nerve

CPAP Continuous positive airway pressure

CRP C-reactive protein
CSF Cerebrospinal fluid
CT Computed tomography

CTA Computed tomographic angiogram
CTV Computed tomographic venogram

DES Dry eye syndrome
EBV Epstein–Barr virus
ED Emergency department
EMG Electromyography
ENT Ear, nose, and throat

ESR Erythrocyte sedimentation rate

FTA-ABS Fluorescent treponemal antibody absorption

GCA Giant cell arteritis
GON Greater occipital nerve

xxii Abbreviations

GPA Granulomatosis with polyangiitis

Hg Mercury

HHV Human herpes virus

HIV Human immunodeficiency virus
HLA Human leukocyte antigen
HPI History of present illness

HSV Herpes simplex virus

ICHD International Classification of Headache Disorders

IgG Immunoglobulin G IgM Immunoglobulin M

IIH Idiopathic intracranial hypertension

IOP Intraocular pressure

IV Intravenous

IVIG Intravenous gamma globulin

kg Kilogram

LASIK Laser in situ keratomileusis

LDS Latter Day Saints

LE Left eye

LP Light perception or lumbar puncture

LUL Left upper lid mg Milligram (s)

MIDAS Migraine Inventory Disability Assessment Score

mL Milliliter(s) mm Millimeter(s)

MOH Medication overuse headache

MR Magnetic resonance

MRA Magnetic resonance angiogram
MRI Magnetic resonance imaging
MRV Magnetic resonance venography

NMO Neuromyelitis optica

NOVEL Neuro-ophthalmology Virtual Educational Library

NSAIDS Nonsteroidal anti-inflammatory drugs

OD Right eye

OIS Ocular ischemic syndrome

OS Left eye OU Both eyes

p-ANCA Perinuclear antineutrophil cytoplasmic antibodies

Pcomm Posterior communicating PCR Polymerase chain reaction

PD Prism diopter

PEK Punctate epithelial keratopathy PET Positron emission tomography

POTS Postural orthostatic tachycardia syndrome

prn As needed

PSP Progressive supranuclear palsy

Abbreviations xxiii

PST Pulse synchronous tinnitus

RAI Radioactive iodine

RAPD Relative afferent pupillary defect

RCVS Reversible cerebral vasoconstriction syndrome

RE Right eye

RF Rheumatoid factor
RNA Ribonucleic acid
RNFL Retinal nerve fiber layer

RNFL Retinal nerve fiber layer
RPR Rapid plasma reagin
SOV Superior ophthalmic vein

SR Sustained release

SSA Sjögren syndrome-related antigen A SSB Sjögren syndrome-related antigen B SSRI Selective serotonin reuptake inhibitor

SUNA Short unilateral neuralgiform headache attacks

SUNCT Short unilateral neuralgiform headache attacks with conjunctival

injection and tearing

TAC Trigeminal autonomic cephalgia

TB Tuberculosis
TBUT Tear break up time
TED Thyroid eye disease
TMJ Temporomandibular joint
TRAB Thyroid receptor antibody

TSI Thyroid-stimulating immunoglobulin

TVL Transient vision loss

u Units

VDRL Venereal Disease Research Laboratory

VZV Varicella zoster virus WHO World Health Organization

x/d Times per day

Part I Ophthalmic Disorders Causing Eye Pain: Relatively Normal Examination

Case 1

History of Present Illness

A 63-year-old woman with a history of strabismus status-post childhood corrective surgery describes pain in both eyes for the last 6 months. She describes an aching pain that is absent when she first awakens then worsens as the day progresses. It is symmetric, daily, and is getting worse occurring more frequently and earlier in the day. She was given eye exercises and prisms without improvement. Nothing initiates the pain, but reading seems to worsen it. Closing her eyes makes it better. Over-the-counter NSAIDs are not beneficial. She endorses occasional redness and occasional tearing. The pain has an aching quality, does not radiate, and measures three out of ten at its worst. She denies blurred vision, ptosis, photophobia, and diplopia.

Past medical and ocular history	Past surgical history
Osteoarthritis	Total knee arthroplasty
Atrial fibrillation	Family history
Depression	Mother—Progressive supranuclear palsy
Hyperlipidemia	Review of systems
Hypertension	Easy bruising
Right-sided congestive heart failure	
Rosacea	
Medications	Social history
Furosemide	One glass of wine daily
Sertraline	No smoking or drug use
Metoprolol	Retired professor
Warfarin	
Vitamin D	
Spironolactone	
Atorvastatin	

1 Case 1

Examination

Acuity with correction

Right eye: 20/20 distance and near Left eye: 20/25 distance, 20/20 near

Pupils

Equal, round, reactive, without an afferent pupillary defect

Intraocular pressure Right eye: 17 mmHg Left eye: 18 mmHg

External exam

Rosacea, mild ptosis of the left upper lid

Eye alignment and motility

Normal motility
Orthophoric in distance
3 PD exophoria at near

Convergence amplitudes 30 PD for distance, 40 PD near

Near point of convergence to nose

Slit lamp examination

Blepharitis

Mild nuclear sclerosis

Tear break up time 4 s BE

No foreign body seen

Visual field Normal

Fundus examination

Normal

Neurologic examination

Normal

Discussion

Ophthalmic Perspective: Dr. Lee

The fact that the pain is intermittent, bilateral, and symmetric would argue away from a fixed orbital process, where I would expect the pain to be constant and unilateral. There are no other features of orbital inflammation such as persistent or worsening redness, proptosis, or chemosis. Her pain is not present in the morning and worsens as the day goes on suggesting this is not a more sinister process. While the patient has a small eye misalignment (exodeviation), this would not constitute a convergence insufficiency (CI). Typically, the deviation in CI (see Case 4) is 10 prism diopters greater at near than distance. Her exodeviation is too small to really call it CI. The patient has very normal convergence amplitudes, well over what is needed to overcome the small misalignment at near. Her near point of convergence is also normal. Although her symptoms are worse with reading, which could suggest CI, she has tried prisms and convergence exercises without benefit.

The mild pain and aching quality sound most consistent with dry eye syndrome (DES). It is important to note that DES is the most common cause of eye pain! In

Discussion 5

my experience, most patients with dry eye-related pain describe generally mild, aching, pressure, or pulling sensation. Some say it radiates behind the eye and others say eye movement worsens it. It would be highly unusual for DES to cause sharp, stabbing or pounding pain or for it to be severe. Many patients note that the pain seems to wax and wane with the day. When patients wake up, their corneas have been protected all night and then become painful with exposure to wind and evaporation especially with reading. Interestingly, sometimes DES pain is unilateral. Many patients will note other symptoms of DES such as burning, blurry vision, tearing, redness, and foreign body sensation but not all will. Examination may show punctate epithelial erosions, early tear break up time (TBUT), blepharitis, or abnormal Schirmer's tear testing (Fig. 1.1). In other cases, the slit lamp examination can appear quite unremarkable. In many, a topical anesthetic will greatly improve the pain. However, patients with chronic DES-related eye pain of several months duration may not enjoy improvement. This occurs because of upregulation of pain modulating proteins within the cornea. Looking at her medications, she is on two diuretics, a beta blocker and a SSRI, which may worsen DES.

We know that she has rosacea, blepharitis, and an early TBUT. Rosacea can cause inflammation of the eyelid margin and disruption of the meibomian glands, which reduces tear quality. We could see if a topical anesthetic substantially improves the pain. We could also measure her tear production. Given the strong history and physical, I would favor treating with artificial tears $4-6 \times /\text{day}$, washing the eyelids with hot water, using warm compresses, fish oil or flaxseed oil (omega 3 oils) $2 \times /\text{day}$ for 1 month then $1 \times /\text{day}$, humidifying her environment, and drinking a lot of water. At bedtime, the patient can also use ocular ointment. If this does not benefit her, then I would add topical corticosteroids $3-4 \times /\text{day}$ tapering by one drop each week. If she had improvement, but not resolution with the corticosteroids, then I would try topical cyclosporine $2 \times /\text{d}$. I would also consider punctal plugs and doxycycline 100 mg $2 \times /\text{day}$. More extreme measures could include scleral contact lenses, which put a layer of tears between the lens and the cornea, or even autologous serum eye drops.



Fig. 1.1 Schirmer tear testing. Some practitioners put anesthetic in and others do not. The strips are placed in the lower fornix and left there for 5 min. After they are removed the degree of wetting is measured using a ruler. Less than 5 mm is considered significantly reduced

6 1 Case 1

Neurologic Perspective: Dr. Digre

I agree with Dr. Lee, that this is dry eye. There are many conditions to at least consider that could be co-morbid in this patient. I would want to be sure she does not have underlying migraine. While she is 63 years old, her migraines may have tapered off, but individuals with previous migraine could be more susceptible to the pain of dry eyes. In addition, in my practice, dry eyes can worsen migraine patient's headaches. I would also be sure that she has no other neurological symptoms. Her mother had progressive supranuclear palsy (PSP) and degenerative neurological disorders can be associated with decreased blinking. While it is not known to be inherited, movement disorders such as PSP and Parkinson disease are frequently associated with both dry eyes and complaints about reading and mild convergence insufficiency. Finally, I would also ask about dry mouth as a symptom of Sjögren's disease which often affects middle-aged women. I frequently do a Schirmer's test. While this is sometimes negative, even when I know the patient has dry eyes, it is often helpful to know how dry the eyes are. As for other testing, if she had dry mouth, I might draw Anti SS A (Anti Ro) and Anti SS B (Anti La) antibodies often seen with Sjögren's disease. Because these labs can be negative with Sjögren's disease, I would consider lip biopsy, if I were very suspicious.

With the lack of any other neurological symptom or examination finding, I would not recommend an MRI scan for this patient. Setting out a written treatment plan is often helpful—outlining the steps to take in improving dry eyes. We frequently recommend warm soaks if there is blepharitis, frequent preservative free tears, and gels or ointments at night. Following up with the patient is also important since further treatment may be helpful. The importance of treating this now and getting DES under control is that, left untreated, this can lead to trigeminal nerve damage and neuropathic pain, resulting in more severe pain, which is much more difficult to treat, so primary prevention of further damage is important.

Non-ophthalmic/Non-neurologic Perspective

The history here will most likely lead you to the diagnosis. You may or may not have a topical anesthetic in the office or emergency room. The pain, if it is going to resolve, will do so within a minute. Staining the cornea with fluorescein may show small, punctate dots of green (aka punctate epithelial erosions or keratopathy) consistent with dry eye. You can use the blue filter on the slit lamp if you have one or, on the direct ophthalmoscope, view the cornea using the +10 lens (green 10). Generally speaking, the visual acuity should be normal or near normal (20/25).

Artificial tears are over the counter. There are two kinds, those with preservatives and those without preservatives. Either one can be used, but some patients develop sensitivity to the preservatives. When asking the patient to wash the eyelids with hot water, this is directed at rubbing gently along the base of the eyelashes where the

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meibomian glands sit. A warm wash cloth over the eyes is also effective. We often ask patients to do this in the shower. We would not favor a non-ophthalmologist giving out corticosteroid eye drops or a topical anesthetic to take home. There are too many risks with an incorrect diagnosis. We would recommend a referral to an ophthalmologist for a correct diagnosis.

Follow Up

The patient's pain resolved with topical anesthetic in the office. She used artificial tears and lid hygiene regularly. The pain persisted, and she tried topical corticosteroids. These did not help substantially. With continued use of the artificial tears and eyelid hygiene and humidification of her environment, her pain resolved spontaneously over several months time. *Final Diagnosis: Dry eye syndrome*.

For Further Study

- Jackson WB. Management of dysfunctional tear syndrome: a Canadian consensus. Can J Ophthalmol. 2009;44(4):385–94.
- Lemp MA. Advances in understanding and managing dry eye disease. Am J Ophthalmol. 2008;146(3):350–6.
- 3. Messmer EM. The pathophysiology, diagnosis, and treatment of dry eye disease. Dtsch Arztebl Int. 2015;112(5):71–81.

Case 2

History of Present Illness

A 75-year-old woman complains of bilateral eye pain. She describes the pain as burning, itching, and constant. Approximately every few weeks, when she awakes she has severe right eye pain. She describes it as sharp with a foreign body sensation, and her vision seems blurred at that time. The pain seems to happen as soon as she opens her eye and she is afraid to open her eyes in the morning. Both the blur and the pain resolve slowly over a few hours. With these sharp pains, her eye waters and it appears reddened. A hot towel and artificial tears make this feel better. The left eye seems normal otherwise. She denies any history of trauma or contact lens use.

Past medical and ocular history	Past surgical history
Hypercholesterolemia	Cataract surgery BE
Osteoarthritis	Blepharoplasty BE
Atrial fibrillation	Tonsillectomy
Anxiety	Tubal ligation
Reflux	Gallbladder removal
Hypertension	Family history None
Medications	Review of systems
Pravastatin	Longstanding joint pain, seasonal allergies, anxiety
Escitalopram	Social history
Losartan	Never smoked, no alcohol, homemaker
Estradiol	
Omeprazole	
Zolpidem	
Warfarin	

10 2 Case 2

Examination

Acuity with correction Right eye: 20/20 Left eye: 20/20

Pupils

Equal, round, briskly reactive, no APD

Intraocular pressure Right eye: 19 mmHg Left eye: 17 mmHg

External exam

3 mm ptosis right upper lid 2 mm ptosis left upper lid

Eye movements

Normal

Slit lamp examination

Anterior basement membrane dystrophy (ABMD) BE

Punctate epithelial keratopathy (PEK) BE

Intraocular lenses BE

Visual field

Normal

Fundus examination

Mild drusen consistent with macular degeneration

Neurologic examination

Normal

Discussion

Ophthalmic Perspective: Dr. Lee

Previously, in Case 1 we discussed dry eye. The patient has signs PEK and symptoms (constant burning and itching) of dry eye syndrome. I believe this is the cause of the constant dull pain that she describes. It almost sounds like she has corneal abrasions but she likely is not scratching her right eye while she is asleep several times.

However, dry eye syndrome (see Case 1) typically feels better in the morning and it does not cause sharp, acute pain. We should examine the patient for lagophthalmos (eyes still partially open after closing gently), which can cause pain in the morning, but the exposure keratopathy of lagophthalmos usually does not cause severe, sharp pain. This scenario above would be most consistent with recurrent corneal erosions. Most commonly, a patient notes a history of corneal abrasion with a sharp object such as a paper cut or a fingernail. The abrasion elevates a layer of the corneal epithelium, which does not cement itself back down well. When patients sleep, the eyelid dries to and sticks to the corneal epithelium slightly. When the patient opens their eye, the eyelid pulls that unstable epithelium off—hence the severe eye pain. This classically improves over a few hours. Oftentimes, the patient