Letting Go of Cognitive Error When Presumed Glaucoma Isn’t Glaucoma: a Teaching Case Report

Anterior Uveitis, More than a Red Eye: a Teaching Case Report

Ocular and Visual Manifestations of Parkinson’s Disease: a Teaching Case Report

Bowen’s Disease of the Eyelid: a Teaching Case Report

Understanding Geographic Atrophy in Advanced Non-Exudative Age-Related Macular Degeneration: a Teaching Case Report

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Educator’s Toolkit: UDL - A Framework for Meeting Diverse Learning Needs

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The demographics of students entering post-secondary education are changing. Today’s students have diverse backgrounds. They are more likely than in the past to be first-generation college students, military students, nontraditional (e.g., older) students, minorities or English language learners. Additionally, more students with disabilities are enrolling in colleges and universities. Studies and other data documenting these demographic shifts are cited throughout the literature, including by Boothe et al., McGuire et al. and Scanlon et al. Diverse learners have diverse learning needs and face various barriers to learning successfully.

This increasingly diverse population of post-secondary students is the applicant pool for schools and colleges of optometry. Therefore, it becomes more important than ever for optometric educators to decrease barriers to learning so the instructional needs of all optometry students continue to be met. While compliance with the federal Americans with Disabilities Act of 1990 and section 504 of the Rehabilitation Act of 1973 remains mandatory, UDL provides an enhanced approach as it can meet the learning needs of a wider range of students.

The UDL Framework

Based on the science of how people learn, UDL is a teaching framework designed to provide a flexible learning environment to meet the needs of diverse students. Applying UDL principles to instructional settings reduces learning barriers by providing instructional environments that are more accessible and effective for students.

UDL was developed in 1984 and has been defined as “a set of principles for curriculum development that gives all individuals equal opportunities to learn.” UDL employs the universal design concept from architecture, which holds that tools and buildings should be accessible to everyone. Similarly, instructional techniques, strategies, materials and activities should be accessible to everyone. The three primary principles of UDL are 1) engagement, 2) representation, and 3) action and expression. Engagement (the why of learning) refers to stimulating motivation and interest in multiple ways. Representation (the what of learning) refers to presenting and collecting information and content in multiple ways. Action and expression (the how of learning) refer to allowing learners alternative ways to navigate the learning environment and demonstrate knowledge.

Figure 1 provides a fundamental description of UDL. CAST, the nonprofit education research and development organization that created the UDL framework, has published guidelines to assist educators with implementation. The guidelines contain cross-discipline suggestions for ensuring learners can access and participate in learning activities (Figure 2). Additional detailed information can be found in the interactive UDL guidelines graphic organizer. With its UDL Rising to Equity initiative, CAST is currently updating the UDL guidelines to redress systemic barriers to equitable learning access and outcomes.
Changes Can Be Incremental

The goal of implementing the UDL framework is to design learning experiences that consider learner variability and eliminate unnecessary barriers to learning. Although developing inclusive learning environments can be a daunting task, it is possible to begin by incorporating relatively simple and minimally time-consuming changes (Table 1). Additional course changes can be made incrementally over time.

More resources pertaining to UDL and UDL implementation are below.

Links to Additional UDL Resources

WEBSITES

- About Universal Design for Learning
- The IRIS Center
- UDL Toolkit by Fred Cochran
- Accessibility of Electronic and Information Technology (for compliance with Rehabilitation Act, section 508)
- Web Content Accessibility Guidelines, (WCAG) 2.1 (for compliance with Rehabilitation Act, section 508)

PODCASTS

- Think UDL, Hosted by Lillian Nave
- The UDL Approach, Hosted by Loui Lord Nelson, PhD

TEXTS

References

Celebrating Teaching Case Reports
Aurora Denial, OD, FAAO, DAAO (OE) | Optometric Education: Volume 47 Number 2 (Winter-Spring 2022)

This edition of Optometric Education celebrates teaching case reports. The concept of teaching case reports for this journal was developed by Barry Kran, OD, FAAO, from the New England College of Optometry, and Elizabeth Hoppe, OD, MPH, DRPH, former editor of the journal. The first two teaching case reports — Management of Anisometropic Amblyopia and Head Posture in a Patient With Oculocutaneous Albinism by Dr. Kran and A Case of Bilateral Ocular Ischemic Syndrome by Andrea L. Murphy, OD, Richard Frick, OD, FAAO, and Dorothy Hitchmoth, OD, FAAO — were published in the winter 2009 edition. Since 2009, the journal has published 64 teaching case reports. I commend Drs. Hoppe and Kran for developing this creative merger, which has benefited faculty, students and clinicians.

A teaching case report combines an interesting clinical case with teaching elements. It is a teaching experience and a learning experience. Teaching case reports represent a collection of cases that are researched, organized and peer-reviewed. The cases can be used in a didactic classroom, clinical setting or in the remediation of students. Little did we know that in 2020 they would also be used to augment students’ clinical experiences during a global pandemic.

Writing a successful teaching case report is within the grasp of all clinical faculty. To get started, authors should identify an interesting prospective case. The case should demonstrate clinical importance and relevance. Authors should discern why the chosen case or learning is important to a student’s academic career. Authors should read the description of teaching case report elements below and consult the Optometric Education publication guidelines, which contain additional important information about content, presentation and format. Knowing this information before writing and submitting saves time and minimizes revisions. In addition, authors should search through published teaching case reports and not waste time writing about a topic that is similar to what has been published recently. The goal is to create a collection of cases that represent a diversity of ocular conditions. (Access the archive by clicking on OPTOMETRIC EDUCATION in the navigation bar at the journal’s website.)

Elements of a Teaching Case Report

The required elements of a teaching case report are background, case description, education guidelines, discussion, conclusion and references.

Background: The background is a brief introduction to the case. It contains the intended audience, relevance of the case (“so what?” and “who cares?”), along with background information on the ocular condition/disease presented in the case. The intended audience may be identified for the entire case. In some complex cases, the intended audience may differ for different aspects of the case.

Case description: The case description is the presentation of the case. The author should hold all aspects of discussion until the education guidelines or discussion section. This allows educators to extrapolate data from the case without having to dissect out discussion comments. Tables, graphs, diagrams and pictures are usually helpful. Original test results, e.g., visual fields and optical coherence tomography, are encouraged. Patients should be described as a person not a case, and patient confidentiality should be respected at all times.

Education guidelines: This section includes the teaching components of the case report, i.e., the information needed to facilitate a discussion of the case. The teaching components are the learning objectives, key concepts, discussion points (questions to facilitate discussion), teaching methodology and assessment (how the learning objectives will be assessed).

Discussion: The discussion section is the vehicle for teaching the case. It should reflect clinical as well as education elements.
Teaching methodology and discussion points should drive the discussion. The discussion section should include a summary and interpretation of key findings, comparison to known findings in the literature, how and why decisions were made and, if applicable, what lessons are to be learned from this experience.

Conclusion: The conclusion summarizes the case and learning experience.

References: References should be listed in the order they are cited in the text. They should be cited in the text by superscript numbers. National Library of Medicine reference style should be used.

Also, teaching case reports should be submitted with an abstract of approximately 100 words and approximately five key words that reflect the primary subject matter of the paper to assist reference librarians and others in retrieval and cross-indexing. Acknowledgments and disclosures should also be included if applicable.

A Valuable Opportunity for All Faculty

Teaching case reports are peer-reviewed publications. They provide faculty the opportunity to showcase their clinical acumen as well as teaching methodology and creativity. At many institutions, a published teaching case report can be a valuable asset in a portfolio for promotion or tenure. It provides insight and understanding regarding teaching philosophy. Because many faculty are not formally trained in education, writing a teaching case report provides a learning opportunity for the author. All faculty who are engaged in patient care and teaching should consider this opportunity and write a teaching case report.
In Response to “Review of Standardized Testing in Doctoral Health Professions Admission Requirements”

Steven H. Schwartz, OD, PhD | Optometric Education: Volume 47 Number 2 (Winter-Spring 2022)

The role that standardized exams should play in optometry program admissions is a timely and important topic, and Ooley et al. (2021) are to be commended for their comprehensive review of usage of such exams by doctoral-level health professions programs. Their paper, “Review of Standardized Testing in Doctoral Health Professions Admission Requirements,” was published in the Fall 2021 edition of Optometric Education. Of the 11 professions (not including optometry) included in their survey, only graduates of medical (allopathic and osteopathic), dental and podiatry programs are licensed to both diagnose and medically treat disease in humans. Data included in the paper indicate that all the educational programs for these professions require the completion of standardized exams for admission.

Optometrists, like the professionals cited above, are licensed in all states to independently diagnose disease in humans and prescribe medications for treatment. Moreover, in at least five states, optometrists may be licensed to perform certain laser procedures, and at least nine states permit minor surgery. When looking for peer professions that may serve as models for optometry school admissions requirements, an important consideration should be whether the profession is granted the responsibility to diagnose and medically treat disease in humans. As is evident in the list of professions listed in the authors’ paper, most doctoral-level healthcare professions do not have this scope of practice and, consequently, these professions do not serve as appropriate peers for this type of analysis.

While Ooley et al. (2021) point out that pharmacists may provide injections and independently dispense contraceptives in certain states, these professionals are not licensed to diagnose and medically treat disease. It is of note that applications to pharmacy programs have plummeted in recent years. The extent to which this is a factor in the absence of a requirement for standardized admissions exams is not clear.

In a companion paper in the Fall 2021 issue of Optometric Education, the predictive utility of standardized admissions exams is discussed, particularly with respect to the lack of published papers for optometry. This is an important issue that deserves more attention. Analysis regarding the continued usage of standardized admissions exams in optometry should, nonetheless, focus on comparisons with professions that have been granted comparable professional responsibilities — namely medicine, dentistry and podiatry, which all currently require completion of standardized exams for admission to their programs. Elimination of such a requirement at this time would make optometry an outlier when compared to these peer professions.

References

Letting Go of Cognitive Error When Presumed Glaucoma Isn’t Glaucoma: a Teaching Case Report

Anney K. Joseph, OD, FAAO | Optometric Education: Volume 47 Number 2 (Winter-Spring 2022)

PDF of Article

Background

Graber et al. describe three major categories of diagnostic errors in medicine: 1) no-fault errors, 2) system errors, and 3) cognitive errors.¹ No-fault errors occur when a disease lacks the classic textbook presentation and/or mimics something more common. System errors occur due to deficiencies in the healthcare system. These include organizational structure, culture, policies, resources, communication and performance detractors. Cognitive errors occur due to perception. This includes faulty data collection or interpretation, inaccurate clinical reasoning or incomplete knowledge.¹ This case report focuses on cognitive error.

Croskerry has published numerous articles about cognitive errors, or cognitive dispositions to respond (CDRs). These CDRs are associated with failures in perception, failed heuristics and biases. A partial list of CDRs may be found in Croskerry’s article “The Importance of Cognitive Errors in Diagnosis and Strategies to Minimize Them.” Recognizing CDRs is key in reducing them. Metacognition is a reflective approach in which one steps back from the “immediate problem to examine and reflect on the thinking process.”²

Eyecare professionals rely on optic nerve appearance, intraocular pressure (IOP), retinal nerve fiber layer (RNFL) quality, visual fields and gonioscopy when monitoring the progression of glaucomatous eye disease. Other disorders of the optic nerve may mimic glaucoma. If misdiagnosed as glaucoma, these disorders can have severe consequences for the patient, both visually and possibly systemically.

Nonglaucomatous disorders that may mimic glaucomatous optic neuropathy include hereditary optic neuropathies, optic nerve infarctions, trauma, infection, demyelinating optic neuritis, fusiform enlargement of the intracranial carotid artery, and intraorbital and intracranial mass lesions.³

Patients with compressive injury may exhibit visual field defects that resemble those of a glaucoma patient. However, when an optic nerve appears to have more pallor than cupping, particularly of the temporal rim, it should prompt third- and fourth-year optometry student clinicians, optometry residents and practicing optometrists to forgo their biases and explore etiologies other than glaucoma.

Case Description

On April 22, 2015, a 65-year-old Vietnamese female presented with a chief complaint of longstanding blurry vision in her left eye and no vision through her right eye. She had been using bimatoprost 0.03% ophthalmic solution, which had been prescribed in Vietnam, in both eyes at bedtime “for many years.” This was her first eye examination in the United States. No previous ophthalmic records were provided by the patient, and she was a poor historian. She reported being supplied with the ophthalmic medication from family and friends returning from Vietnam. (In many countries, a prescription is not necessary to purchase medication.) A Vietnamese interpreter was used during the examination via telephone.

The patient’s medical history was significant for diabetes mellitus, hypertension and hyperlipidemia. Her medications included metformin 1,000 mg, fenofibrate nanocrystallized 145 mg, glipizide 10 mg, lisinopril 20 mg, metoprolol tartate 25 mg and atorvastatin 20 mg.

Her pertinent laboratory tests as of Feb. 17, 2015, were hemoglobin A1c 8.0% and total cholesterol 207 mg/dL with 62 mg/dL high-density lipoprotein. Her blood pressure on March 2, 2015, was 130/60 and her body mass index was 25.71 kg/m2. The patient was oriented to person, place and time, and her mood and affect were appropriate.

On examination, the patient’s unaided visual acuities were no light perception (NLP) in the right eye and 20/320 in the left eye improving with pinhole to 20/80. Pinhole testing of the right eye with NLP was deemed unnecessary as this was the initial eye examination. Pupils were equally round and reactive to light with a relative afferent pupillary defect in the right eye. Confrontation visual fields were not possible for the right eye due to NLP vision and full to finger count in the left eye. Ocular
motilities were full range of motion with no restriction in either eye. Ishihara color vision test results were 0/8 plates with the right eye and 8/8 plates with the left eye. Refraction revealed no improvement in the right eye with any lens change and +3.00 +1.25 x 030 in the left eye resulting in 20/70 distance visual acuity.

Slit lamp biomicroscopy examination was remarkable for patent peripheral iridotomy and nuclear sclerotic cataract in both eyes. IOP measured 14 mmHg in both eyes via Goldmann applanation tonometry. Corneal pachymetry measurements were 540 µm in the right eye and 535 µm in the left eye. Sussman four-mirror gonioscopy of both eyes revealed posterior trabecular meshwork in all four quadrants with 1-2+ pigment and no peripheral anterior synechia or neovascularization of the angle.

Dilated fundus examination was remarkable for pallor of the right optic nerve, with cup-to-disc ratio of 0.1 and distinct disc margins. The left optic nerve showed no pallor, distinct margins and cup-to-disc ratio of 0.15 (Figure 1). There was an epiretinal membrane over the macula of the right eye. The left eye was unremarkable.

Magnetic resonance imaging (MRI) of the brain and orbits was ordered. Bimatoprost was discontinued, and brimonidine 0.15% ophthalmic solution 3 times daily in both eyes was prescribed for its neuroprotective potential. The patient was counseled to keep her blood sugar, blood pressure and cholesterol under control. The epiretinal membrane was not visually significant. The cataract in the left eye was visually significant; however, the patient elected to defer cataract surgery. A spectacle prescription was dispensed.

MRI of brain and orbit (Figure 2) was performed on May 11, 2015, and revealed a right medial sphenoid wing meningioma described by the radiologist as an “extensive, invasive extra-axial mass centered in the region of the right cavernous sinus/Meckel’s cave with involvement of the right orbit, encasement of the right optic nerve and right ICA.” Although exophthalmos was not clinically evident, proptosis of the right eye was noted on MRI. The amount of proptosis was measured radiologically via exophthalmos index (EI). On scans, globe protrusion is defined as greater than 21 mm from the interzygomatic line (IZL) to the anterior surface of the globe or less than 9.9 mm from the IZL to the posterior sclera margin. The ratio between this measurement in the affected eye vs. the normal eye is defined as the EI, and any number greater than 1.0 indicates proptosis. The EI for this patient was 1.17.

A consultation with neurosurgery on June 5, 2015, confirmed the diagnosis of meningioma. Follow-up appointments with neurosurgery on June 26, 2015, and Nov. 20, 2015, revealed no changes in the patient’s status. Therefore, it was determined that the patient would need only surgical decompression if the left visual acuity were to become compromised. The patient returned to the eye clinic for Humphrey visual field testing of the left eye, and optical coherence tomography (OCT) of the RNFL was performed on both eyes. Results are shown in Figures 3 and 4. Visual acuity and IOP at this visit remained stable. Five months later, on Oct. 14, 2015, the patient had a follow-up MRI of her brain, which showed no interval changes.
Figure 1. The patient’s IRIS retinal camera optic nerve photographs. It is difficult to appreciate the pallor of the right optic nerve (top); however, note the lack of significant cupping. The left fundus (bottom) was unremarkable. Click to enlarge

Figure 2. MRI showing large homogeneous enhancing mass centered in the right cavernous sinus/Meckel’s cave extending anteriorly through the superior orbital fissure into the posterior right orbit. The yellow horizontal arrow is the interzygomatic line. Exophthalmos index (EI) is defined as $a$ (mm)/$b$ (mm). In this example, $EI = 21 \text{ mm}/18 \text{ mm} = 1.17$. Click to enlarge
Figure 3. Humphrey visual field 30-2 of the left eye showing inferior edge defects with no optic neuropathy noted.
Click to enlarge

Figure 4. OCT of the right and left eye retinal nerve fiber layers. Note the significant atrophy of the right optic nerve.
Click to enlarge

Education Guidelines

Key concepts

1. Recognize the clinical signs of compressive nonglaucomatous optic neuropathy vs. glaucomatous optic neuropathy
2. Recognize visual field defects in compressive nonglaucomatous optic neuropathy vs. glaucomatous optic neuropathy
3. Recognize ancillary tests that aid in the diagnosis of compressive nonglaucomatous optic neuropathy and the importance of reviewing the medical record and history
4. Understand co-managing patients with compressive nonglaucomatous optic neuropathy, including treatment and follow-up
5. Understand CDRs and the need to investigate further if the clinical picture does not match a diagnosis (diagnosis momentum)

Learning objectives

At the conclusion of this case discussion, participants should be able to:

1. Describe the typical presentation of compressive nonglaucomatous optic neuropathy vs. glaucomatous optic neuropathy
2. Understand the clinical findings associated with compressive nonglaucomatous optic nerve damage and differential diagnoses
3. Understand how to use ancillary testing to aid in diagnosis and prognosis of compressive nonglaucomatous optic neuropathy and potential complications
4. Describe treatment and team management of compressive nonglaucomatous optic neuropathy
5. Acknowledge and set aside cognitive biases to minimize diagnostic errors

Discussion questions

1. Does compressive nonglaucomatous optic neuropathy affect vision?
2. Does compressive nonglaucomatous optic neuropathy affect pupil response?
3. What are other clinical signs of compressive nonglaucomatous optic neuropathy?
4. What differential diagnoses should be considered in cases of suspected compressive nonglaucomatous optic neuropathy?
5. What ancillary testing can aid in the diagnosis of compressive nonglaucomatous optic neuropathy?
6. What is the appropriate management for compressive nonglaucomatous optic neuropathy?
7. What is the prognosis for compressive nonglaucomatous optic neuropathy?
8. What role did cognitive error play in this case?

Learning assessment

1. Facilitate case discussion to achieve learning objectives
2. Knowledge base can be evaluated by comparing fundus photographs and visual fields of glaucomatous vs. nonglaucomatous optic neuropathy
3. Knowledge base of the condition and clinical-thinking skills can be assessed via student presentations of differential diagnoses and ancillary tests to rule out those diagnoses

Discussion

Teaching instructions

Clinicians and students using this teaching case report should read each discussion question and think about how they would respond and compare and contrast with the information provided below. Participants may work together in small groups or individually. Learning objectives are to be assessed by comparing participants’ responses with the information provided. This case may also be presented as a PowerPoint lecture comparing and contrasting fundus photographs and visual fields in nonglaucomatous optic neuropathies with glaucomatous optic neuropathy. It may also be presented as a case discussion in a journal club setting.

Does compressive nonglaucomatous optic neuropathy affect vision?

Visual acuity can be normal or impaired depending on whether the central visual field is affected. Best-corrected visual acuity is typically 20/40 or worse in patients with suspected compressive lesions. Vision loss is gradual, not sudden. This compares with best-corrected visual acuity of 20/20, which is typical for glaucoma patients until late- to end-stage glaucoma. Be wary of asymmetric decreased visual acuity. In addition, it is critical to investigate the cause of vision loss, even NLP vision, as a patient’s ocular and systemic health may be at risk as is shown in this case.

Does compressive nonglaucomatous optic neuropathy affect pupil response?

A relative afferent pupillary defect (RAPD) can be detected by performing the swinging light pupil test. In the presence of bilateral symmetric optic neuropathy or early stage compressive lesion not affecting the optic nerve, RAPD may be absent. The briskness of pupillary constriction to light will reflect the degree of optic nerve dysfunction. When checking for RAPD, it is important to use a very bright light in a dark room to assess the full amplitude of pupillary response.

What are other clinical signs of compressive nonglaucomatous optic neuropathy?

The ocular manifestations of sphenoid wing meningiomas vary depending on the size and location of the primary tumor. The classic triad of signs is proptosis, decreased vision (Snellen visual acuity worse than 20/40) and impaired extraocular motility. Other signs may be temporal fullness and globe displacement, which can present in orbital or temporal fossa masses. Tumors near the sella or optic nerve can cause visual field defects (that border the vertical midline) and optic disc edema or atrophy (without cupping of the disc). Ptosis, eyelid edema, chemosis, diplopia and loss of facial sensation may also present.

Compare and contrast these signs with the clinical signs of glaucomatous optic neuropathy, which are better Snellen visual acuity, visual field defects that border the horizontal midline, older age of patient at presentation, vertical elongation of the optic cup, peripapillary atrophy and, occasionally, splinter disc hemorrhages.

| Table 1. Click to enlarge |
**Table 1** is a quick reference guide for signs and symptoms of compressive nonglaucomatous vs. glaucomatous optic neuropathy.

What differential diagnoses should be considered in cases of suspected compressive nonglaucomatous optic neuropathy?

Differential diagnosis of optic neuropathy includes any etiology that may cause damage to the optic nerve. A pale optic disc indicates a longstanding complication such as compressive, hereditary or toxic/nutritional neuropathies. Optic nerve pallor may also indicate sequelae of an acute inflammatory or ischemic optic neuropathy. Sectoral pallor with retinal attenuation should alert the clinician to previous nonarteritic ischemic optic neuropathy (NAION). A careful review of history (rapid vs. gradual onset, associated symptoms, medical conditions, age/gender predilection) and thorough ophthalmic evaluation narrows potential diagnoses.

This is a unique case in that the patient, as a female of Asian descent, may have had narrow angles on gonioscopy at her initial eye examination in Vietnam and deemed at risk for an angle closure attack necessitating laser peripheral iridotomy (LPI). Literature review shows that close follow-up and further medications and/or laser or surgery post LPI is necessary to prevent progression of the disease in Vietnamese patients, which would validate the anti-glaucoma medication this patient had been taking. In a prospective observational case series, Shen et al. reported on changes in optic disc morphology (increased cup-to-disc ratio and decreased mean neuroretinal rim area) from week 2 to week 16 post LPI in subjects with acute primary angle closure. This patient’s previous eye exams and procedures were performed in Vietnam; therefore, requesting records was impossible. Within the range of differentials for this patient, any diagnosis along the primary angle closure spectrum could be plausible except for the lack of cupping of the optic nerve in either eye. This case shows that progressive, painless, unilateral vision loss with optic atrophy in the absence of cupping is not glaucoma. In a retrospective study, Trobe et al. reported that pallor of the neuroretinal rim is 94% specific in predicting nonglaucomatous optic neuropathy.

Theoretically, one may also consider functional vision loss, or nonorganic vision loss (NOVL), when a new patient presents with NLP vision. NOVL is described as decreased visual acuity and/or visual field loss not caused by an organic lesion/pathology and diagnosed after a complete neuro-ophthalmic examination. It can run the spectrum from malingering to subconscious vision loss secondary to underlying psychological disorder, typically depression or anxiety. Few in-office techniques can help to differentiate NOVL from pathology. On confrontation or tangent screen visual field testing, remember that normal visual field is a funnel, not a tunnel. A patient’s constricted visual field should expand when the test moves from 1 meter to 2 meters away. If the constricted visual field remains the same at 1 meter and 2 meters, that is tunnel vision and consistent with NOVL. Typical automated visual field presentation is a cloverleaf or square pattern in NOVL. Pupil testing will be unremarkable in a patient presenting with NOVL vs. a positive RAPD in patients with true pathology. Upon color vision testing with pseudoisochromatic plates, a patient presenting with NOVL will often report not seeing the test plate. Contrast sensitivity testing in NOVL is variable and inconsistent, which supports the diagnosis of NOVL. Simple tests of proprioception can also be used to rule out NOVL. For example, a patient with true, organic vision loss can bring their index fingertips together in front of them whereas a patient with NOVL will be unable to do so, thinking the exercise is vision-dependent.

What ancillary testing can aid in the diagnosis of compressive nonglaucomatous optic neuropathy?

Visual field defects that respect the vertical meridian on formal testing should alert the clinician of possible compression or infiltration. Visual field testing also aids in localization of the lesion. A hemianopic defect indicates a lesion at or posterior to the chiasm. A junctional scotoma, an ipsilateral central field defect and contralateral superotemporal field defect, indicates a compressive lesion at the junction of the optic nerve and the chiasm.

Color vision testing via pseudoisochromatic test plates such as Ishihara color plates or American Optical Hardy-Rand-Rittler (AOHRR) color plates can indicate optic nerve damage. Most patients with acquired optic neuropathy will have some degree of dyschromatopsia. The AOHRR test has an advantage over the Ishihara test with acquired color deficiencies, in particular with optic neuropathies, with its inclusion of plates designed to test for S-cone mechanism defects. Glaucoma first causes an acquired S-mechanism deficiency and later, in advanced disease, it causes an acquired M-L mechanism deficiency. Red cap desaturation is another quick clinical tool to assess optic neuropathy. A positive response would be that the red cap color appears “faded” or “pink” in the eye with optic nerve damage vs. “red” in the eye with no optic nerve damage.

OCT uses light to penetrate tissue and analyzes the reflected image of the optic nerve head and the peripapillary RNFL. It can also play a role in predicting recovery in patients with severe compressive neuropathy. Loo et al. found that patients with compressive optic neuropathy due to anterior pathway meningiomas are more likely to improve after treatment if they have a normal pretreatment peripapillary RNFL and shorter duration of symptoms.

Exophthalmometry should be performed when patients present with proptosis. Approximately 44% of patients with compressive optic neuropathy have proptosis less than 4 mm, and roughly 35% have proptosis greater than 4 mm. People of
Asian decent typically have Hertel exophthalmometry measurements between 16 and 18 mm; people of African decent typically have measurements between 20 and 22 mm; and people of Caucasian decent typically have measurements between 18 and 20 mm. The difference between a patient’s two eyes usually does not exceed 2 mm. As referenced above, the amount of proptosis may also be measured radiologically, utilizing either computed tomography or MRI scans. Symmetry between ocular globes correlates to an EI of 1.0; any number greater than 1.0 indicates some degree of proptosis.

Contrast sensitivity is usually reduced in patients with optic neuropathy and may be tested using the Pelli-Robson chart. Contrast sensitivity reduction may be detected prior to Snellen visual acuity reduction.

MRI of the brain and orbit is essential in diagnosing compressive lesions. The two most common intracranial mass lesions that cause optic nerve pallor are pituitary lesions at 57.1% and meningiomas at 21.4%. Pituitary adenomas have the classic bitemporal hemianopsia seen on formal visual field testing. Meningiomas are the most common primary tumor of the central nervous system, accounting for approximately 33.8% of all brain tumors. They occur more commonly in older, female populations. Sphenoid wing meningiomas constitute 11-20% of intracranial meningiomas and those with secondary orbital extension are rare. These tumors are compressive and slow-growing at a rate of 1 to 3 mm per year. Sphenoid wing meningiomas can involve the region of the anterior clinoid process, adjacent medial sphenoid wing, superior orbital fissure and cavernous sinus. They are classified as either globoid tumors with a nodular shape or an en plaque tumor, which is flat and spreads along the entire sphenoid ridge. The globoid tumors are further broken down into three groups depending on their location: inner (medial), middle and lateral. Medial sphenoid wing meningiomas have a higher morbidity, mortality and recurrence rate due to their involvement with anterior visual pathways, anterior intracranial arteries and the cavernous sinus. As the tumor becomes larger, it may encase the internal carotid and proximal middle and anterior cerebral arteries. The optic nerve may also be compressed if it is surrounded by the tumor resulting in vision loss and visual field defects. Neurologic deficits or seizures may present in patients with large tumors that put pressure on the frontal and temporal lobes and provoke edema in the adjacent brain tissue.

What is the appropriate management for compressive non-glaucomatous optic neuropathy?

The treatment avenues for meningiomas involve observation (as in this patient’s case), surgery, radiation and chemotherapy. General guidelines for the treatment of meningioma indicate that it may be appropriate to follow patients with mild or nonprogressive symptoms with periodic MRI and examination to determine whether the lesion is growing and if symptoms are significantly interfering with the patient's life. Surgical intervention is often preferred for younger patients with worsening symptoms and/or growth seen on follow-up scans. The indications for surgery in older patients are a large tumor with worsening symptoms. Radiation therapy is used in older patients with small and medium size tumors with worsening symptoms and for treatment of regrowth after subtotal or radical subtotal removal. Chemotherapy is used as a treatment option in meningiomas that are progressive, recurrent or inoperable. Typically, it does not play a significant role in management of meningiomas due to significant systemic toxicity encountered with chemotherapy and modest to no tumor regression detected.

A critical factor for aggressive tumors is angiogenesis, which is mediated by vascular endothelial growth factor (VEGF). Therefore, bevacizumab, a humanized monoclonal antibody against VEGF-A, has been used in the treatment of recurrent or progressive meningiomas resistant to standard therapy.

Tumor recurrence is the major risk in the long run; thus, in most initial surgeries, aggressive resection is advocated. The size of the tumor affects the extent of tumor removal and determines clinical outcomes including visual acuity recovery.

Meningiomas often invade the optic canal. In addition to tumor excision, optic canal decompression optimizes visual outcomes as well as lowers the chances of tumor recurrence. Early decompression of the optic nerve within the bony canal allows identification and separation of the tumor from the nerve, permitting removal of the tumor from this area with minimal manipulation of the optic nerve, thus providing better visual prognosis.

What is the prognosis for compressive non-glaucomatous optic neuropathy?

Overall, the potential for malignancy is low for sphenoid wing meningiomas. Cornelius et al. found in a large retrospective study of patients who were operated on for meningioma, 90% of the tumors were benign. Recurrence rate of meningioma after treatment with surgery, radiation or combined therapy is approximately 10%. Morbidity from the tumor and therapeutic interventions depends on the location of the tumor and proximity to vital neurological and ocular structures.

In general, visual prognosis has been shown to be dependent on preoperative visual acuity and extent of tumor surgical resection. Trends show that early surgical intervention may benefit patients before visual decline starts. Studies also support radical resection on the first surgical encounter to minimize residual tumor, propensity for recurrence and need for repeat
surgery, all of which have a negative visual outcome.\textsuperscript{31}

What role did cognitive error play in this case?

Types of CDRs that played a role in perpetuating the glaucoma diagnosis in this patient were anchoring, confirmation bias, diagnosis momentum, premature closure and search satisfying. Anchoring is the “tendency to lock onto salient features in the patient’s initial presentation too early in the diagnostic process, and failing to adjust this initial impression in the light of later information.” Confirmation bias is the “tendency to look for confirming evidence to support a diagnosis rather than look for disconfirming evidence to refute it, despite the latter often being more persuasive and definitive.” Diagnosis momentum refers to a diagnostic label that gets “stickier and stickier” through continued use by patients, nurses, physicians, paramedics. It becomes so sticky that what was once a possible diagnosis becomes definite and all other possibilities are excluded. Premature closure is similar to diagnosis momentum in that it accepts a diagnosis prior to being fully verified; “when the diagnosis is made, the thinking stops.” Search satisfying is akin to diagnosis momentum and premature closure. This is the “universal tendency to call off a search once something is found.” The risk in stopping the search is that comorbidities may be missed.\textsuperscript{2}

Conclusion

Previous articles describe intracranial masses that mimic glaucomatous cupping; however, this is a case where there was no glaucomatous cupping, yet the patient was being treated for glaucoma. While sphenoid wing meningiomas are slow-growing tumors, they are compressive and involve ocular structures, making timing of diagnosis essential in the visual prognosis for patients. If an optic nerve appears to have pallor in excess of cupping, refer for imaging. Prompt intervention may limit permanent disability from these tumors. When clinical signs do not match the presenting diagnoses, it is imperative that eyecare professionals let go of their cognitive dispositions to respond and investigate further.

References

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Anterior Uveitis, More than a Red Eye: a Teaching Case Report
Allison Cronin, OD, FAAO | Optometric Education: Volume 47 Number 2 (Winter-Spring 2022)

PDF of Article

Background

Uveitis is, by strict definition, an inflammation of the uveal tract. The term can also be used to describe many other forms of intraocular inflammation involving not only the uvea but also the retina and its vasculature. The uveal tract is divided into anterior and posterior portions. The anterior portion of the uveal tract consists of the iris, while the posterior portion contains the ciliary body as well as the choroid. Uveitis can be classified in many different ways, all dependent on what part of the eye is affected: anterior uveitis occurs when the iris and/or the pars plicata of the ciliary body is involved; intermediate uveitis involves the pars plana, the peripheral retina and the vitreous; posterior uveitis involves the fundus posterior to the vitreous base; panuveitis involves the entire uveal tract; endophthalmitis involves all intraocular tissues except the sclera; and panophthalmitis involves the entire globe. Anterior uveitis is the most common form of uveitis, followed by posterior, intermediate and finally panuveitis.

The diagnosis of anterior uveitis is based on inflammation limited to the anterior chamber. Diagnosis and management require a thorough case history and collection of detailed history of present illness, as well as review of systems, in order to uncover any potential systemic conditions that could contribute to the development of the uveitic episode. Standard ophthalmic treatment for anterior uveitis includes a topical steroid with slow taper once the inflammation has resolved. Cycloplegic drops are also used for pain management, the prevention of posterior synechiae formation and, in extreme cases, the formation of iris bombé. All ocular treatment strategies are focused on reducing symptoms, controlling inflammation, minimizing treatment complications and preserving vision. Observing the course of the disease and response to treatment can provide additional insights into identifying a cause for the episode. Additional laboratory tests may be indicated if the uveitis is bilateral, granulomatous or recurrent. The most common vision-threatening complications of uveitis include macular edema, cataract and glaucoma.

This teaching case report highlights the appropriate management of a patient with a severe, persistent presentation of anterior uveitis. It is intended for third- and fourth-year optometry students actively involved in clinical patient care. Because this ocular condition can be intimately related to systemic health, sound knowledge of anterior uveitis as well as the systemic conditions associated with it is essential for the practicing optometrist in a clinical environment. This case can be used as a teaching tool in a didactic setting and it can be utilized in clinical seminars focused on patient care.

Case Description

A 30-year-old Turkish male presented to the clinic as an emergency walk-in on a Friday morning complaining of a persistent red eye for the past 3 weeks. His only symptoms consisted of a constantly red right eye and occasional watering. He denied any recent illness, contact with someone else having a red eye, light sensitivity, discharge, pain or noticeable changes in vision. He denied any previous contact lens wear. He reported that he had gone to the Student Health Center a few weeks ago when he first noticed the redness and he was given a prescription for ciprofloxacin. He experienced no improvement with ciprofloxacin so he went back to the health center and was given a prescription for polymyxin B and trimethoprim ophthalmic (Polytrim). He failed to see any improvement with Polytrim so he presented to the clinic. The patient’s most recent eye exam prior to the appointment was 7 months earlier and there were no remarkable findings at that exam. His ocular history was unremarkable. His medical history was unremarkable and he was not taking any medications, prescribed or over the counter, at the time. His family ocular history was unremarkable. His family medical history was positive for diabetes mellitus, cancer and heart disease. Social history was positive for occasional alcohol consumption, and he denied use of tobacco products. He denied any allergies to medications. He was a full-time student at the time of this exam. He was oriented to time, place and person, and his mood was appropriate.

Entering uncorrected visual acuities at distance were 20/80 in the right eye (OD) and 20/25 in the left eye (OS). Pupils were equal in size, 4 mm OD and OS measured in bright room illumination, round and reactive to light, with no signs of an afferent pupillary defect in both eyes (OU). There was a slightly sluggish direct and consensual response to light observed OD when compared to OS. Extraocular motilities were smooth and exhibited full range of motion OU. Cover test revealed orthophoria at
distance and 4x exophoria at near. Confrontation visual fields were full to finger counting in each eye. Best-corrected visual acuities with refraction were 20/25-2 OD and 20/20 OS at distance. Intraocular pressure (IOP) measured with Goldmann applanation tonometry was 36 mmHg and 19 mmHg at 11:31 a.m. in the right and left eye, respectively. IOPs from his exam 7 months ago were checked and measured (with Goldmann) 16 mmHg and 18 mmHg in the right and left eye, respectively.

Anterior segment exam with slit lamp biomicroscopy revealed normal adnexa, lids, lashes and puncta in both eyes. In the right eye, 1+ diffuse bulbar conjunctival injection as well as 2+ perilimbal injection were observed. Also noted in the right eye were diffuse corneal edema and diffuse endothelial mutton fat keratic precipitates (KPs), coalesced inferiorly (Figure 1). No mucus discharge was observed, and there was no significant papillary reaction observed within the palpebral conjunctiva. The anterior chamber of the right eye was difficult to accurately assess for cells and flare due to diffuse corneal edema, but cells and flare were determined to be present. The corneal edema also made it difficult to obtain clear views of the posterior segment during the dilated exam. Though significant vitreal haze was observed, it was not possible to document the presence of intermediate or posterior uveitis at this visit. B-scan ultrasonography would have provided further assessment of the posterior segment of the right eye; however, there was no B-scan equipment available in the clinic. Optical coherence tomography (OCT) of the posterior segment was not pursued due to the significant corneal edema and vitreal haze that would have correlated with poor image quality and poor reliability. Gonioscopy might have revealed additional information; however, due to the emergent presentation and time constraints of this case, it was not performed. The left eye presented with unremarkable findings, including a clear cornea and quiet bulbar and palpebral conjunctiva. Undilated examination of the posterior segment OS showed normal findings to the extent seen: clear crystalline lens, flat and intact macula, normal vasculature, and well-perfused optic nerve with cup-t-disc ratio of 0.35/0.35.

Differential diagnosis for the persistent red eye included bacterial conjunctivitis, viral conjunctivitis, anterior uveitis, bacterial keratitis and infectious endophthalmitis. Bacterial conjunctivitis was ruled out due to lack of mucus discharge, papillary reaction, and lack of improvement with previous topical antibiotic treatment. Viral conjunctivitis was excluded due to lack of palpebral conjunctival follicles. Bacterial keratitis was ruled out because no epithelial defect was present, no infiltrate was observed during slit lamp examination, and no evidence of epithelial staining with fluorescein was seen. Infectious endophthalmitis was excluded mostly due to the patient’s denial of any prior surgical procedure. Eye pain, hypopyon, eyelid edema and chemosis were also absent.

The diagnosis for the persistent red right eye was anterior uveitis. One drop of brimonidine tartrate/timolol maleate ophthalmic solution (Combigan) and one drop of homatropine were instilled in the office in the right eye only. Prescriptions for prednisolone acetate 1% (Pred Forte 1%) every hour while awake OD only and Combigan twice daily every 12 hours OD only were provided. The patient was instructed to get the prescriptions filled as soon as possible. He was instructed to return to the clinic the next day for IOP monitoring and compliance with medications. It would have been beneficial to check the patient’s IOP after instillation of Combigan to ensure it was effectively lowering IOP, but the patient refused to wait in office and declined the procedure despite being educated on the importance of assessment. Because the patient was scheduled to return to the clinic the following morning, it was decided not to force him to wait for an IOP check that afternoon.

The patient returned to the clinic the following day for his second examination and he reported no change in symptoms. His symptoms included a red right eye; however, he did not complain of light sensitivity, pain or changes in vision. He reported good compliance with topical medications. Uncorrected visual acuities at distance had improved slightly to 20/50 OD and 20/20-2 OS. Pupils were unequal in size, but the right eye was still dilated from homatropine instillation at the previous exam. There was a very small reaction to light OD, but this small reaction was most likely due to the dilation performed the previous day. Pupillary response OS was normal. Extraocular motilities were smooth with full range of motion OU. Best-corrected distance visual acuities with refraction were 20/25-2 OD and 20/20 OS, no improvement with pinhole OD. The most likely cause of the patient’s reduced acuities was secondary to the significant organic disruption of the anterior segment including corneal edema, diffusely scattered KPs and the presence of dense cells and flare in the anterior chamber. IOP was still elevated in the
right eye despite the use of Combigan. Goldmann applanation tonometry revealed 36 mmHg and 19 mmHg IOP at 8:34 a.m. in the right and left eye, respectively. There was no change in the presentation of the anterior segment OD, and the posterior segment still could not be clearly viewed. Due to the persistent elevation of IOP OD, the patient was given four tablets of acetazolamide 250 mg (Diamox). He was instructed to take one tablet twice a day for 2 days. The use of an additional topical medication to lower IOP was not utilized at this time because there were no other IOP-lowering drops available in the clinic and the patient reported he was unable to afford additional topical medications due to insufficient medical insurance coverage.

Dorzolamide (Trusopt) was considered as an additional drop for treatment; however, given the patient’s financial situation, the oral treatment available in-office was ultimately pursued. The patient’s IOP was not checked after the first tablet of Diamox was administered because he refused to stay in the office for further assessment. It would have been beneficial to ensure IOP was decreasing, and the patient was educated on the importance of assessment; however, because the patient was instructed to return in 2 days and to call the emergency care line if any changes or new pain occurred, it was determined not to be necessary to force the patient to wait for an IOP check after he declined. The patient received a strong loading dose of Pred Forte 1% after the first examination, and the prescription was changed from every hour while awake to every 2 hours OD only while awake. A prescription for atropine was also provided to maintain cycloplegia, and the patient was initially instructed to use one drop of atropine once weekly OD only. The duration of atropine 1% is typically 7-10 days so this original prescription was intended for once weekly use but was subject to change based on the patient’s response and compliance. It was possible that the duration of action of atropine could be reduced due to the severe inflammation the eye exhibited, but given the patient’s financial situation it was unknown if the drop would be purchased at all. The original instruction for once weekly use was potentially under-prescribed, but the goal was to avoid overuse until his reaction to the drop was determined. Atropine was prescribed rather than homatropine due to the severe inflammatory reaction observed in the affected eye and the longer duration of action. The patient was instructed to return to the clinic in 2 days.

He returned to the clinic 2 days later for his third examination and reported that the redness had resolved. The patient said he was still using his medications as directed. At this point he was still using Pred Forte 1% every 2 hours and Combigan twice daily OD only. The patient denied filling the atropine prescription due to financial reasons. Uncorrected visual acuities at distance, 20/40-2 OD and 20/20-2 OS, showed signs of improvement. Extraocular motilities were still smooth with full range of motion OU. Pupils showed minimal change with pupil size 6 mm OD and 4 mm OS in bright room illumination. The right pupil was still slightly larger, most likely due to homatropine. Duration of action for homatropine can be up to 72 hours. Both pupils were reactive to light with the right eye exhibiting a sluggish reaction. Best-corrected visual acuities with refraction were 20/20 OD and 20/20 OS. IOP measurements with Goldmann applanation tonometry revealed 11 mmHg and 14 mmHg in the right and left eye, respectively. Slit lamp exam with biomicroscopy revealed minimal improvement; however, the anterior chamber and posterior segment of the right eye were able to be examined at this visit due to mild reduction of the corneal haze. The cornea still exhibited signs of mild edema and the mutton fat KP’s were still diffusely scattered, coalescing inferiorly. There was 1+ cells and 2+ flare in the anterior chamber. Grading the anterior chamber cells and flare was accomplished using the Standardization of Uveitis Nomenclature (SUN) Working Group grading schemes. Posterior segment examination revealed no signs of intermediate or posterior uveitis. The posterior segment exam did not reveal vitreous cells, vitreous haze, white exudative material in the peripheral retina, or retinal or choroidal inflammatory lesions. The macula was flat and intact and the optic nerve was well perfused with 0.40/0.40 cup-to-disc ratio. One drop of homatropine was instilled in office OD only because the patient had not filled the prescription for atropine. Diamox use was discontinued due to regulated IOP OU, but the patient was instructed to continue using Combigan twice daily OD only. He was instructed to continue using Pred Forte 1% every 2 hours while awake OD only. The patient was instructed to return to the clinic in 5 days.

The fourth examination 5 days later revealed significant improvements. The patient presented with no symptoms or complaints. He denied redness, pain, light sensitivity and changes in vision. He reported good compliance with the medications and stated that he was still using Pred Forte 1% and Combigan as directed. He did not fill his prescription for atropine. Uncorrected visual acuities at distance were 20/25-2 OD and 20/20-2 OS. Best-corrected visual acuities at distance with refraction were 20/20 OD and OS. Pupils were equal, round and reactive to light with no signs of an afferent pupillary defect OU. The reaction to light OD was no longer sluggish and appeared equal to that of OS. Extraocular motilities were smooth with full range of motion OU. IOP with Goldmann applanation tonometry was measured to be 18 mmHg and 17 mmHg OD and OS, respectively, at 9:18 a.m. Anterior segment exam showed significant signs of improvement with a reduced amount of mutton fat KP’s distributed across the endothelium. Corneal edema had almost completely resolved. Cells in the anterior chamber had reduced from 1+ to trace and flare had decreased from 2+ to 1+. Dilated posterior segment exam, using one drop of tropicamide 1% and one drop of phenylephrine 2.5%, was unremarkable and did not show signs of inflammation that would indicate an intermediate or posterior uveitis. Dilated examination of the posterior segment OS was also unremarkable. The patient was instructed to begin taper of the topical steroid medication. He was instructed to continue use of Pred Forte 1% 4 times daily OD only. He was also instructed to continue use of Combigan twice daily OD only. He was also escorted to the office building next door at the conclusion of this exam for lab testing due to the granulomatous nature of the condition. Several lab tests were ordered: complete blood count (CBC) with differential/platelet, human leukocyte antigen B27 (HLA-B27) disease
The patient returned to the clinic 2 weeks later for his fifth examination. He had no symptoms or complaints. He reported good compliance with the medications, using Pred Forte 1% 4 times daily and Combigan twice daily OD only. Uncorrected visual acuities at distance were 20/25 OD and 20/20-2 OS. Best-corrected visual acuities at distance with refraction were 20/20 OD and OS. Because the manifest refractions performed at the fourth and fifth exams were stable and nearly identical, a prescription for glasses was provided to the patient, but he reported that he was happy with his vision and would most likely not fill the prescription. Pupils were equal, round and reactive to light OU with no signs of an afferent pupillary defect. Extraocular motilities were smooth with full range of motion OU. IOP measured with Goldmann appplanation tonometry was 17 mm Hg and 18 mm Hg at 10:06 a.m. OD and OS, respectively. Corneal edema was completely resolved. Mutton fat KPs were almost completely resolved with a few scattered inferiorly and their inferior placement was not visually significant. No cells or flare were present in the anterior chamber. The patient was instructed to continue taper of topical steroid. He was instructed to use Pred Forte 1% 3 times daily for 1 week, 2 times daily for 1 week, and then to discontinue use completely. He was instructed to continue using Combigan twice daily until he was finished using Pred Forte 1% and to then discontinue.

The patient’s lab results were also reviewed during the examination and each test came back within normal limits and unremarkable: CBC with differentials was within normal limits, HLA-B27 was negative, ACE was within normal limits, Lyme was negative, VDRL screening test was normal, toxoplasma gondii antibody was negative, RF was within normal limits, ANA was negative, RPR was non-reactive, and FTA-ABS was non-reactive. He was instructed to return to the clinic in 4 weeks. He returned to the clinic 4 weeks later for his sixth examination with no complaints and complete resolution of anterior uveitis.

Three weeks following the patient’s sixth and final examination, the patient returned to the clinic with complaints of a red right eye. He reported that the redness had started 2 days prior. He denied complaints of light sensitivity, pain or changes in vision. He stated that he considered starting the previously prescribed drops again but he decided to return to the clinic before using any of the medications. Ocular and medical histories were reviewed but remained unchanged. Uncorrected visual acuities at distance were 20/40+1 OD and 20/20-1 OS. Pupils were equal, round and reactive to light with no signs of an afferent pupillary defect OU. Extraocular motilities were smooth with full range of motion OU. Best-corrected visual acuities at distance with refraction were 20/25+2 OD and 20/20 OS. Anterior segment exam with slit lamp biomicroscopy revealed 2+ perilimbal injection OD, mild diffuse corneal edema OD, and 2+ cells and 2+ flare in the anterior chamber OD. There were no KPs present OD. OS anterior segment examination was unremarkable. IOP measured with Goldmann appplanation tonometry was 32 mmHg and 18 mmHg at 11:04 a.m. OD and OS, respectively. Dilated examination of the posterior segment using tropicamide 1% and phenylephrine 2.5% was unremarkable OU. The diagnosis at this time was recurrent anterior uveitis OD. One drop of Combigan and one drop of homatropine were instilled in-office OD only. The patient was instructed to begin treatment again using one drop of Pred Forte 1% every 2 hours while awake and to use one drop of Combigan twice daily OD only. A new prescription was provided for the patient to purchase additional topical medication as needed. The patient was also given four tablets of Diamox and was instructed to take one tablet twice daily for 2 days. He was told to return to the clinic in 2 days.

The patient returned to the clinic 2 days later with improved symptoms. He reported that the redness had improved, and he denied any pain, photophobia and changes in vision. Uncorrected visual acuities at distance were 20/30+3 OD and 20/20-2 OS. Pupils were equal, round and reactive to light with no signs of an afferent pupillary defect OU. Extraocular motilities were smooth with full range of motion. Best-corrected visual acuities with refraction were 20/20 OD and OS. IOP measured with Goldmann appplanation tonometry was 32 mmHg and 14 mmHg at 1:52 p.m. OD and OS, respectively. Anterior segment exam revealed trace diffuse bulbar conjunctival injection, resolved corneal edema, trace cells in the anterior chamber, resolved flare in the anterior chamber, and an absence of KPs. Dilated exam using tropicamide 1% and phenylephrine 2.5% was unremarkable. Given the patient’s previous success with treatment, he was instructed to continue using Pred Forte 1% 4 times daily and Combigan twice daily OD only for 2 weeks. Diamox tablets were discontinued. The patient was instructed to return to the clinic in 2 weeks.

He returned to the clinic 2 weeks later with no complaints and reported good compliance with the topical medications. Uncorrected visual acuities at distance were 20/25+1 OD and 20/20-2 OS. Pupils were equal, round and reactive to light with no signs of an afferent pupillary defect OU. Extraocular motilities were smooth with full range of motion OU. Best-corrected visual acuities at distance with refraction were 20/20 OD and OS. IOP measured with Goldmann appplanation tonometry was 17 mmHg and 19 mmHg at 2:06 p.m. OD and OS, respectively. Anterior segment exam was unremarkable with complete resolution of conjunctival injection, corneal edema, cells and flare OD. Given the normal and negative results of the lab workup and the relatively quick onset of the second occurrence after discontinuing topical treatment, it was determined that this...
The patient was instructed to continue using Pred Forte 1% 4 times daily for 2 weeks, then 3 times daily for 3 weeks, then 2 times daily for 2 weeks, then 1 time daily for 2 weeks, then 1 time daily every other day for 2 weeks, and then to discontinue. He was also instructed to continue use of Combigan twice daily every day while still using Pred Forte 1%. He was instructed to return to the clinic in 12-14 weeks, or sooner if the symptoms returned.

He returned to the clinic 12 weeks later with complete resolution. He reported that he followed the directions for the topical medications and did not have any flare-ups. Uncorrected visual acuities at distance were 20/25 OD and 20/20-2 OS. Pupils and extraocular motilities were normal OU. IOP measured with Goldmann applanation tonometry was 18 mmHg and 17 mmHg at 9:04 a.m. OD and OS, respectively. Anterior segment and posterior segment examinations were unremarkable OD and OS. Extensive education about the condition was reviewed with the patient and he was told that another round of lab tests may be necessary, as well as other potential tests, if the condition returned in the right eye or occurred in the left eye. A complete physical was recommended to the patient but he denied having a primary care provider at the time. The importance of a chest X-ray was discussed with the patient and he reported that as soon as he found a physician he would return to the clinic for a referral. There was also a discussion about possible referral to a rheumatologist should the condition return.

**Education Guidelines**

The following discussion points and literature review help facilitate discussion of the case and management of anterior uveitis. Additional information regarding systemic associations and appropriate laboratory testing is included to further educate the clinician.

**Learning objectives**

At the conclusion of this case discussion, students should be able to:

1. Recognize the signs and symptoms of anterior uveitis
2. Understand the differences between granulomatous and nongranulomatous anterior uveitis
3. Identify the systemic conditions associated with anterior uveitis and know which laboratory tests to order to investigate each systemic condition

**Key concepts**

1. Recognition of clinical signs and reported symptoms associated with anterior uveitis
2. Understand how to manage anterior uveitis
3. Knowledge of the systemic conditions and additional laboratory work associated with anterior uveitis

**Discussion points**

1. Clinical presentation of anterior uveitis
2. Describe common symptoms of acute anterior uveitis
3. Discuss the differences between acute, chronic, recurrent and resistant uveitis
4. Describe basic clinical signs of anterior uveitis
5. Additional exercise: create a list of appropriate questions to ask a patient when investigating a chief complaint of “red eye”
6. Clinical treatment and management
7. Discuss the clinical signs of anterior uveitis that warrant additional laboratory testing
8. Describe the differences in presentation and in systemic associations between granulomatous and nongranulomatous anterior uveitis
9. Discuss a treatment plan for an acute anterior uveitis patient with and without elevated IOP
10. Discuss topical and oral treatment options for lowering elevated IOP
11. Create an appropriate laboratory workup referral for a patient who presents with unilateral, granulomatous anterior uveitis
12. Discuss the clinical presentation and potential symptoms of a patient who presents with anterior uveitis and has an underlying systemic condition (perform this exercise with at least three different systemic conditions)

**Assessment of knowledge**

Additional methods of assessing the students’ mastery of content can include:
Quiz containing questions focused on discussion topics

1. Randomizing the systemic conditions, ocular signs and blood work/laboratory tests presented in Table 1 in a matching activity and requiring the students to accurately match the correct systemic condition to ocular signs and blood work/laboratory tests

2. Requiring the students to create their own laboratory referral (or complete an established laboratory referral form for a local clinical laboratory) indicating the tests that should be ordered for an anterior uveitis case that requires additional systemic tests. The students should indicate the systemic condition associated with each test

Discussion

Pathophysiology

Acute anterior uveitis is generally characterized by cells and flare in the anterior chamber, ciliary flush and KPs. The hallmark sign of an anterior uveitis is the detection of leukocytes within the aqueous humor of the anterior chamber. Symptoms associated with acute anterior uveitis include sudden onset of unilateral deep ocular pain, redness, photophobia, excessive tearing and reduced vision; some cases are relatively asymptomatic. Symptoms may be mild or absent in patients with chronic anterior uveitis. The pain arises from structures inside the globe, commonly as a consequence of inflammation of uveal structures, which is typically also associated with photophobia. Pain after inflammation of the uveal tract is due to enhanced activity in the abundant polymodal nociceptor fibers innervating the uveal structures. The mechanism for the photophobia experienced is uncertain, but reflex contraction of the ciliary and/or iris muscles triggered by light exposure or accommodation may become painful if nociceptor sensory nerve endings in these structures were also sensitized. While photophobia secondary to ciliary muscle spasm is common, it can also be induced by anterior chamber cellular infiltration, corneal epithelial edema and pupillary muscle involvement. The pain associated with anterior uveitis can vary, but it is usually a dull aching type or a throbbing sensation in the eyebrow area. The patient in this case did not complain of pain or light sensitivity, which is potentially unusual for anterior uveitis; however, the patient also did not complain of any visual changes even though visual acuity was reduced to 20/80 in the affected eye. It is possible that the patient had a high pain tolerance and was not significantly affected by any possible painful symptom, or it is possible that the patient did not want to fully disclose his symptoms. His primary concern at all of his visits was the redness in the affected eye, and he did not admit to any other symptom. It is also possible that he may have noticed some form of pain or photophobia at onset but adapted to any discomfort before his initial visit to the clinic 3 weeks later. Additionally, patients who present with a chronic case of anterior uveitis may have mild symptoms or the symptoms may be absent. Onset of acute anterior uveitis is sudden and duration is limited to 3 months or less. In addition to acute uveitis, the condition may be described as chronic, recurrent or resistant. Chronic uveitis describes persistent inflammation characterized by prompt relapse within 3 months after discontinuation of therapy. This patient can be diagnosed with chronic anterior uveitis because he had a prompt relapse of inflammation within 3 months after he discontinued therapy. Recurrent uveitis is characterized by repeated episodes of uveitis separated by periods of inactivity without treatment lasting at least 3 months. Resistant uveitis describes the condition when there is no clinical improvement despite 2 weeks of steroid treatment at maximal dose.

Clinical features may vary on a case by case basis but, as previously mentioned, the hallmark feature is cells in the anterior chamber. Inflammatory cells do not arise in the aqueous itself, so the presence of cells or increased protein (flare) in the aqueous is an immediate sign of anterior uveitis.
Ocular conditions associated with acquired syphilis include a chancre on the eyelid or conjunctiva, uveitis, optic neuritis, active care with a primary care doctor was stressed and discussions about additional testing and imaging took place. A definitive diagnosis of sarcoidosis should the anterior uveitis return to either eye, which is why the importance of follow-up was stressed and discussions about additional testing and imaging took place. The patient did not present with any other physical complaints or signs that might indicate further investigation toward sarcoidosis. A chest X-ray or computed tomography (CT) scan would absolutely be indicated in order to confirm or rule out a posterior or intermediate uveitis reaction. Additionally, the patient did not show any other ocular manifestations that would indicate a posterior or intermediate uveitis reaction. The patient did not present with any other physical complaints or signs that might indicate further investigation toward sarcoidosis. Fine KPs typically cover the entire corneal endothelium and are associated with herpetic disease, Fuchs heterochromic iridocyclitis and cytomegalovirus retinitis. Small nongranulomatous KPs are associated with HLA-B27, trauma, juvenile idiopathic arthritis (JIA), PSS, as well as the granulomatous conditions. Granulomatous KPs are large and greasy in appearance and have been given the term “mutton-fat” KPs. These granulomatous KPs usually coalesce on the inferior cornea and are associated with sarcoidosis, syphilis, tuberculosis (TB), lens-induced changes and Vogt-Koyanagi-Harada syndrome. The patient in this case displayed large granulomatous KPs, which prompted an initial laboratory workup. A nonspecific initial laboratory workup is indicated if the uveitis is bilateral, granulomatous or recurrent.

Systemic associations

Although the majority of patients (approximately 50%) are found to have idiopathic anterior uveitis, it is essential to be aware of the systemic etiologies that could potentially be causing the ocular inflammation. HLA-B27 systemic associations include ankylosing spondylitis (AS), reactive arthritis (Reiter syndrome), psoriatic arthritis and inflammatory bowel disease. HLA-B27-associated uveitis is the most commonly diagnosed cause of acute anterior uveitis. Recurrent, severe, alternating, nongranulomatous anterior uveitis with a higher incidence of posterior synechiae is very characteristic of uveitis episodes associated with HLA-B27 conditions. Fine KPs and endothelial dusting occur, and posterior synechiae are frequently present, but the uveitis is nongranulomatous. Severe anterior chamber reaction with fibrin can occur, and a hypopyon is common as well and is associated with the severity of the systemic disease. The most common symptomatic association of AS and other forms of spondyloarthritis is with acute anterior uveitis. In fact, approximately 25-40% of patients with AS will experience a sudden onset of unilateral anterior uveitis at some point during the course of their disease. Thus, it is especially important to ask patients with anterior uveitis about any inflammatory lower back pain. The patient discussed denied any symptoms of back pain, or other bodily aches or pain, when questioned. He denied any current and previous symptoms of joint pain, as well as any current or previous history of arthritis. The lab results also revealed negative results for HLA-B27 disease association. Given this negative lab result, it was possible to rule out AS, reactive arthritis, psoriatic arthritis, inflammatory bowel disease and other conditions associated with positive HLA-B27.

Ocular manifestations of sarcoidosis include large mutton-fat KPs, iris nodules, anterior and posterior synechiae, sheathing along peripheral retinal veins (candle-wax drippings), peripheral retinal neovascularization, snow balls and vitreous body base condensates. Ocular involvement in sarcoidosis is present in up to 30-60% of patients and is frequently manifested before the systemic disease has been diagnosed. Uveitis is the most common ocular manifestation observed in patients with sarcoidosis, and it can present as anterior, intermediate or posterior. Chest radiography is the most useful test for diagnosing sarcoidosis with the radiographs being abnormal in 90% of patients with the condition. Serum ACE is elevated in 60-90% of patients with active sarcoidosis making it a useful screening test. A biopsy of the lungs can also be performed to provide the greatest accuracy for diagnosis even in asymptomatic patients with normal chest imaging results. Based on the patient’s normal ACE serum levels and on the normal CBC with differentials results, sarcoidosis was tentatively ruled out. The patient also did not show any other ocular manifestations that would indicate a posterior or intermediate uveitis reaction. Additionally, the patient did not present with any other physical complaints or signs that might indicate further investigation toward sarcoidosis. A chest X-ray or computed tomography (CT) scan would absolutely be indicated in order to confirm or rule out a definitive diagnosis of sarcoidosis should the anterior uveitis return to either eye, which is why the importance of follow-up care with a primary care doctor was stressed and discussions about additional testing and imaging took place.

Ocular conditions associated with acquired syphilis include a chancre on the eyelid or conjunctiva, uveitis, optic neuritis, active
The presentation of uveitis secondary to syphilis can be granulomatous or nongranulomatous. Ocular manifestations typically occur during the secondary stage of infection of acquired syphilis. Due to the variable presentation of syphilis, laboratory tests should be performed in all patients with uveitis who require an investigation. Diagnosis of active syphilis requires a combination of treponemal-specific tests and nontreponemal tests. VDRL and RPR screening tests are nontreponemal tests that are best used to diagnose primary infection and to monitor disease activity. The results of the VDRL and RPR tests have a tendency to show negative results in early primary, latent, late stages, as well as 6-18 months after conclusion of therapy for syphilis. Treponemal antibody tests are highly sensitive and specific in all stages of syphilis and more useful for proving past infection. When FTA-ABS results are negative, no treatment is indicated. The result of the FTA-ABS cannot be titrated and is either positive (reactive) or negative (non-reactive). The patient’s VDRL test result was normal (non-reactive), while his FTA-ABS test result was also non-reactive. Based on these two test results, syphilis was ruled out as a possible cause for his uveitis.

Lyme disease is an infection caused by Borrelia burgdorferi, and it can affect any ocular structure. Therefore, it can present with a wide variety of ocular manifestations, including uveitis. Uveitis, while uncommon, can present as anterior, intermediate, peripheral multifocal choroiditis, retinal periphlebitis and neuroretinitis. Intraocular inflammation can occur in both early and late stages of the disease. The characteristic features of anterior Lyme-related uveitis can include granulomatous uveitis, and it is generally bilateral, although unilateral cases have been reported. The patient denied any feelings of malaise or fatigue or flu-like symptoms. However, given the granulomatous appearance of his uveitis, a Lyme disease antibody with reflex to blot (IgG, IgM) was ordered from the laboratory. Interpreting the serology results required careful examination. The Lyme IgG/IgM Ab western blot reflex result came back negative. The Lyme Ab IgM quant result came back high at 0.99 (normal index referencing values 0.00-0.79). However, after further review it was determined that the Lyme IgM western blot result was negative. A positive result would have included two of the following IgM bands: 23, 39 or 41. The patient’s results revealed an absence of all three bands, which indicated a negative result. Lyme IgG western blot results came back as negative as well. There was one IgG antibody present, IgG P45 Ab; however, a positive result requires five Borrelia-specific bands, which was not the case with this patient’s test results.

RF laboratory testing is relatively sensitive for rheumatoid arthritis, and may also be positive in patients with other rheumatic diseases including Sjogren’s syndrome and systemic lupus erythematosus (SLE). ANA is another test that can indicate underlying rheumatic diseases and connective tissue disorders including SLE. The ocular conditions associated with rheumatoid arthritis include dry eye, keratitis and scleritis; however, anterior uveitis is common among individuals with JIA. While it was unlikely that the patient in this case had an undiagnosed form of rheumatoid arthritis or JIA due to lack of systemic and physical symptoms, the laboratory workup did include RF and ANA testing to confirm or rule out these types of conditions. The patient’s lab results came back negative for ANA Direct, and the RF test revealed a normal value that did not indicate the presence of RF.

PSS, also known as recurrent glaucomatocyclic crisis syndrome, is characterized by recurrent episodes of unilateral, acute secondary open-angle glaucoma associated with mild anterior uveitis. PSS predominantly occurs in young to middle-age patients, but it may also be diagnosed in the elderly, and there is a male predilection. The condition itself is rare but it must be considered in the list of differentials in cases of unilateral uveitis associated with elevated IOP. Signs of PSS include significantly elevated IOP (usually 40-60 mmHg), open angle without posterior synechiae, minimal anterior chamber reaction, corneal epithelial edema and few fine KPs located on the central corneal endothelium. PSS was considered as a potential differential diagnosis for the patient’s condition due to his age, sex and elevated IOP; however, it was ruled out based on the patient’s clinical presentation. He presented with granulomatous KPs as well as a significant anterior chamber reaction, both of which contradict the presentation of PSS. Performing a complete glaucoma workup including pachymetry, gonioscopy, OCT and visual field testing could be indicated if the presentation changes.

Ocular involvement occurs in approximately 1-2% of patients with TB. TB can affect the anterior and posterior segments of the eye as well as the ocular adnexa and orbit. TB is most often associated with granulomatous anterior uveitis including mutton-fat KPs, iris nodules and broad posterior synechiae; however, it can also be associated with intense nongranulomatous cases of anterior uveitis. Patients with suspected TB should have a systemic evaluation to check for evidence of the disease including a chest X-ray and tuberculin skin tests. A purified protein derivative (PPD) skin test can be performed to aid in the diagnosis of TB; however, these skin tests are not 100% sensitive or specific for TB and can provide false results. TB blood tests can also be performed to confirm or rule out latent or active TB, but imaging and sputum tests provide the definitive diagnosis. Chest X-rays or CT scans will show white spots in the lungs where the immune system has walled off the TB bacteria. If the chest X-ray or CT scan shows signs of TB, samples of sputum should also be tested for TB bacteria. Unfortunately, the lab that this patient was sent to did not provide PPD skin testing for TB so it was not performed. If the patient had been able to acquire a primary care doctor, additional testing including PPD skin test, chest X-ray or CT scan could have been pursued to effectively confirm
or rule out TB.

Differential diagnoses for anterior granulomatous uveitis include sarcoidosis, syphilis, TB, idiopathic and herpes simplex. Inflammation of the cornea and uveal tract from an infection with varicella zoster virus (VZV) or herpes simplex virus (HSV) is a common cause of anterior uveitis. The ocular inflammation may be due to the viral infection itself or the inflammatory response to the infection. Patients may develop redness, itching, burning and tearing and experience photophobia, moderate to severe pain and blurry vision. It is commonly associated with conjunctival injection, corneal scars, history of unilateral recurrent red eye, decreased corneal sensation, increased IOP (hypertensive uveitis) and sectoral iris atrophy. 

Synechial closure, trabeculitis, a steroid-induced alteration of trabecular meshwork function, extracellular matrix deposition, or a pupillary block are the mechanisms most often observed during the early stages of chronic uveitis that contribute to elevated IOP. Synechial closure, morphological changes in the trabecular meshwork due to infiltrated inflammatory cells, and altered aqueous composition are the mechanisms seen most commonly at a later stage. The patient discussed presented with anterior uveitis that had been ongoing for at least 3 weeks, and his IOP was significantly elevated so it was imperative to reduce the IOP and monitor it closely for any potential signs of secondary glaucoma. Combigan was initially prescribed so that the patient could benefit from the anti-2-agonist qualities of brimonidine as well as the beta-blocker qualities of timolol. A prostaglandin was not considered because the desired effect of IOP-lowering takes longer to achieve and because prostaglandin analogs should be avoided while inflammation is present. Because the patient’s IOP was still significantly elevated after using Combigan, Diamox was utilized to achieve normal IOP more quickly than with topical medication alone. Additionally, oral medication was pursued because the patient could not afford additional topical medications without the help of his insurance. Once the patient’s IOP was regulated, Diamox was discontinued with hope that the lowered IOP could be maintained using only Combigan.

Treatment

Standard treatment for anterior uveitis includes a cycloplegic to assist with pain management as well as a topical steroid to
control inflammation. Cycloplegic drops can also prevent the development of posterior synechiae while reducing the pain associated with ciliary body inflammation and spasm.\textsuperscript{2} Cyclopentolate, homatropine and atropine are the most commonly used cycloplegic agents for the treatment of uveitis.\textsuperscript{17} Homatropine was utilized in-office in this case because it would provide the longest duration of action when compared with tropicamide 1\% and cyclopentolate. Tropicamide duration of action for cycloplegic effect is typically 6-8 hours; cyclopentolate duration of action is typically 24-36 hours; and homatropine duration of action is typically 36-72 hours.\textsuperscript{3,17} Atropine has the longest duration of action for cycloplegic effect and can last up to 7-12 days.\textsuperscript{3,17} Cyclopentolate was not considered for an initial treatment for cycloplegia because it was thought to be too weak for the severe inflammation observed in this case. Additionally, cyclopentolate has a chemotactic effect on leukocytes and may cause a sticky iris in patients with a history of uveitis.\textsuperscript{18} Given the patient’s severe inflammation it was deemed most appropriate to dilate the patient with the longest acting cycloplegic in-office and prescribe atropine for use at home. The patient never filled his prescription for the cycloplegic agent so he was dilated at all of his follow-ups, except for the second exam when he was still dilated from homatropine instillation the previous day, in an attempt to provide cycloplegia for the patient. While the use of cycloplegics in this case was not ideal, it was difficult to provide constant cycloplegia for the patient when he was not able to afford the topical medications for use at home. Most cases of moderate to severe acute uveitis require initial dosing of a topical steroid every 1-2 hours, but dosing may be less frequent depending on the medication being used.\textsuperscript{2,7} If there is no improvement with topical steroid use, systemic corticosteroids as well as systemic immunosuppressive agents may be utilized.\textsuperscript{2} Pred Forte 1\% is commonly used as a topical medication but it requires frequent dosing to be effective, and such frequent dosing can lead to noncompliance among patients.\textsuperscript{6,7} Difluprednate 0.05\% (Durezol) may allow less frequent dosing than Pred Forte 1\% due to its higher potency.\textsuperscript{2} Studies reported Sheppard et al. demonstrated that dosing Durezol 4 times daily was noninferior to Pred Forte 1\% dosed 8 times daily in patients with endogenous anterior uveitis.\textsuperscript{2,6} The patient in this case report was given a prescription for Pred Forte 1\% despite his severe inflammatory reaction because it was more affordable than Durezol. After inflammatory signs were observed to be resolving, a slow taper was initiated. Failure to taper topical steroids may result in a rebound of the condition. Unfortunately, the patient did develop what is believed to be a rebound occurrence shortly after discontinuing all topical medications. This can also be considered a case of chronic anterior uveitis because the uveitis returned within 3 months of discontinuing the treatment. A much longer taper was utilized during the second episode, which safely resolved and has yet to recur.

**Conclusion**

While a systemic etiology for anterior uveitis is not always present, it is essential to be aware of the potential conditions that could cause this inflammatory reaction (Table 1). Topical treatment of anterior uveitis is usually sufficient for resolution; however, additional methods of treatment may be indicated based on the patient’s presentation and systemic conditions. Management of anterior uveitis patients should include careful case history, laboratory testing when indicated and regular supervision to monitor treatment response.

**References**

Ocular and Visual Manifestations of Parkinson’s Disease: a Teaching Case Report

Jolinda Tam, OD, and Pauline F. Ilsen, OD, FAAO | Optometric Education: Volume 47 Number 2 (Winter-Spring 2022)

Background

Parkinson’s Disease (PD) is one of the most common neurodegenerative conditions, just second to Alzheimer’s.1 It was first documented as a neurological syndrome in 1817 by James Parkinson, though symptoms that suggested PD had been described even earlier.2–3 In 1925, Brissaud proposed that damage to the substantia nigra was seen in individuals with PD.2 The substantia nigra is one of the primary sites of dopamine production. Damage to the structure would then result in reduced levels of this neurotransmitter. Clinically, this presents itself as an impairment in motor control. By 1967, Hoehn and Yahr created the first staging system for PD, which was based on the level of clinical disability.2,4 Since then, there has been much advancement in understanding the condition. However, the root cause is still not known and there is no known cure for PD, only ways to treat the symptoms.

Though the motor impairments of PD are well-established, the ocular and visual manifestations are not widely recognized.3,5–8 With a rise in the aging population, it is of great importance that eyecare providers are aware of these findings so they can better care for patients with PD.1 Furthermore, greater dependence is placed on vision to guide patients in daily activities when they have motor dysfunctions.3,6,8

Currently, when individuals are diagnosed with PD, they are already symptomatic with motor impairments. Some findings suggest the disease process has started years before these clinical findings present themselves.1,9–12 Research is now focused on several features, including identification of biomarkers that may allow for early detection of PD, an objective way to monitor for disease progression, and evaluation of novel therapies.5,13 The goal of exploring these features is to someday be able to slow the degenerative changes, if not halt them altogether. Of most interest to eyecare professionals is the retina. Within the inner retinal layer resides the cell bodies of amacrine cells, which contain dopamine. Postmortem examination of patients with PD has revealed decreased levels of dopamine within the retina.14,15 Given this finding, studies have been investigating retinal changes as a potential biomarker for PD.14 Though there have been many studies, there is yet to be a large-scale study with conclusive findings.5,14,15

The following case involves a patient with ocular manifestations of PD whose motor impairment affected his management plan. The intended audience is third- and fourth-year optometry students, residents and current practitioners.

Case Description

A 69-year-old male presented for Humphrey visual field (HVF) 24-2 SITA Fast (SF) testing, intraocular pressure (IOP) check and gonioscopy for follow-up as a glaucoma suspect OD<OS vs. other optic neuropathy OS. The patient was first seen at the eye clinic a little over 1 year ago with an unremarkable ocular history. His medical history was significant for Parkinson’s disease and delirium in remission. Medications included carbidopa 25 mg/levodopa 100 mg (Sinemet, Merck & Co., New Jersey) 1 tablet by mouth every night at bedtime and 1.5 tablets by mouth 5x/day while awake to counteract the motor impairments, entacapone (Comtan, Orion Corporation, Finland) 200 mg 1 tablet by mouth 5x/day while awake to extend the effect of the former drug, and rasagiline mesylate (Azilect, Teva Pharmaceuticals, Israel) 1mg 1 tablet by mouth every day to stabilize movement disorders.
The patient’s best-corrected visual acuities were 20/20 OD and 20/20 OS. Extraocular muscle movements were smooth and unrestricted OU. Pupils were equally round and reactive to light with no afferent pupillary defect and stable physiological anisocoria OD<OS. Confrontation visual fields were full to finger counting OD and OS, and frequency doubling technology (FDT) screening perimetry was noted to be reliable and full OD and OS. Central corneal thickness was measured at 553 µm OD and 544 µm OS by PARK1 non-contact pachymetry.

Clinical evaluation resulted in the following pertinent findings: capped meibomian glands OU, decreased blink rate OU, cup to disc ratio of 0.35 OD and 0.45 OS with mild temporal pallor as noted during the first examination at the clinic about 1 year ago. IOP measured 13 mmHg OD and 15 mmHg OS by Goldmann applanation tonometry. Gonioscopy confirmed open angles, trace trabecular meshwork pigmentation, flat iris approach, and no angle abnormalities OU. HVF 24-2 SF was completed with an overall low reliability. There were excessive maximal gaze errors as seen on the gaze tracker indicating unreliable fixation. The patient was not able to complete visual field testing as a result of tremors, which was why only the right eye was tested at the visit (Figure 1).

The patient’s tremor from PD rapidly worsened throughout the examination to the point that it was no longer controlled. He required near complete assistance in taking his medication and getting out of the examination chair and out of the clinic. The patient was instructed to return to the clinic in 3 months for repeat FDT perimetry, dilated fundus examination and optical coherence tomography (OCT) of the optic nerve. It was recommended that he schedule the next appointment for just after taking medications to ensure better motor control, which would allow a more productive eye examination.

**Education Guidelines**

**Learning objectives**

1. Recognize that PD affects the ocular and visual system in addition to systemic motor function
2. Understand that with the loss in physical stability, those with PD are more dependent on their vision to navigate through everyday life
3. Recognize that research is being done to find a reliable biomarker for PD, and the retina is a candidate

**Key concepts**

1. Ocular and visual manifestations of PD and the eyecare provider’s role in improving the patient’s quality of life
2. Management of patients with eye findings from PD
3. Changes in retinal thickness and eye tracking as potential biomarkers for early detection of PD

**Discussion points**

1. What are the systemic motor and non-motor features of PD? What are the more common ocular disorders arising from PD?
2. What are the pathological characteristics of PD and how do they relate to the eye?
3. What is the clinical syndrome known as “parkinsonism?” What are the differential diagnoses and how would you distinguish them from PD?
4. How should dry eyes be managed in patients with PD?
5. What are possible causes of diplopia in patients with PD and how can it be managed?
6. How should glaucoma be managed in patients with PD?
7. How can contrast sensitivity loss or impairment in color vision be managed in patients with PD?
8. What should be considered if a patient with PD has visuospatial or visuoperceptual impairments?
9. How should visual hallucinations be addressed in patients with PD?

**Literature review**
PD is one of the most common neurodegenerative disorders. Both the incidence and prevalence of PD increase with age. Incidence in the general population is 14 per 100,000 people, and among those 65 years or older the incidence is 160 per 100,000 people. In a review and meta-analysis reported by Marras et al., the prevalence among North Americans age 45 years or older was 572 per 100,000 people in 2010. It was estimated that 680,000 people had PD then. This number was projected to rise to roughly 930,000 by 2020 and to 1,238,000 by 2030 due to the increasing elderly population.

A number of risk factors have been associated with PD, with increasing age being the most significant. There is a strong correlation between aging and rising prevalence of PD, with prevalence more than doubling from 60 to 80 years old. There are studies that have shown an increased risk of PD to be influenced by environment, genetics and lifestyle. These factors include exposure to pesticides, solvents, consumption of dairy products, traumatic brain injury and history of melanoma. Genetics is also thought to play a role, with variants in alpha-synuclein (α-syn) being a notable source.

Discussion

Teaching instruction: Participants should read each question and consider how they would respond. Next, they should read the information provided in the text. Participants may work alone or together in small groups, either in real time or as part of a homework assignment. Learning objectives are to be assessed by comparing participants’ responses to the information provided.

What are the systemic motor and non-motor features of PD? What are the more common ocular disorders arising from PD?

Parkinson’s disease presents with both motor and non-motor symptoms, but it is known primarily as a movement disorder. The classic presentation includes resting tremors, cogwheel rigidity (when movement is jerky rather than smooth), shuffling gait and bradykinesia (slow movement). Non-motor features include cognitive decline, constipation, sleep disturbance and hyposmia (reduced ability to smell things), some of which may precede impairment in motor control. PD also affects the ocular and visual system. The common ocular disorders that have been reported in the literature include dry eyes; abnormalities of eye movement such as pursuits, saccades and vergences; diplopia; glaucoma and glaucoma-like changes such as inner retinal thinning and retinal nerve fiber layer (RNFL) thinning on OCT (controversial); contrast sensitivity loss; impairment in color vision; visuospatial and visuoperceptual impairments; and visual hallucinations.

What are the pathological characteristics of PD and how do they relate to the eye?

Dopamine and the retina

Parkinson’s disease is characterized by reduced dopamine levels caused by destruction of neurons within the substantia nigra, specifically the pars compacta. This decrease in dopamine results in impairment of motor control. Of interest to eyecare professionals is that dopamine is produced by amacrine cells, inter-plexiform cells and retinal pigment epithelial (RPE) cells, which reside within the inner retinal layer. Postmortem examination has revealed decreased levels of dopamine within the retina. Given this finding, studies have been investigating retinal thinning, which can be readily evaluated via OCT, as a potential biomarker for PD. Tsironi et al. and Nowacka et al. found that there is no difference in RNFL thickness between patients with PD vs. a control group. Conversely, Chrysou et al. completed a meta-analysis of spectral-domain OCT studies and concluded that there is inner retinal thinning found in patients with PD, but it was similarly found in patients with glaucoma and other neurodegenerative diseases such as Alzheimer’s. In a prospective study by Kirbas et al., the retina was found to be thinner in patients with PD than in a control group. Likewise, Satue et al. found that the RNFL was remarkably thinner in PD patients than in healthy individuals. Research findings have been inconsistent with regard to which quadrant exhibits the most significant thinning. Inzelberg et al. reported the inferotemporal sector was thinnest, while Matlach et al. implicated the superior quadrant. Kirbas et al. and La Morgia et al. found the temporal quadrant to have the greatest thinning. The inconsistencies among the various results are likely in part due to the lack of large-scale longitudinal analyses.

Alpha-synuclein and the retina

PD is also pathologically characterized by an accumulation of α-syn within Lewy bodies. This protein is of interest as studies have shown that it seems to regulate dopamine release, and overexpression is associated with decreased levels of the neurotransmitter. Aggregates of α-syn are found in those with PD. α-syn has been located in bodily fluids and peripheral tissues, including blood, cerebral spinal fluid (CSF), saliva, gut mucosa and skin. As such, it is also seen as a potential biomarker for PD. Of the aforementioned locations, CSF has shown to be the most promising though it is not as easily obtained and requires a more invasive collection technique compared with collection of other bodily fluids.

Given that α-syn is found in bodily fluids, studies have investigated its ability to cross the blood-brain barrier (BBB).
al. has concluded that it not only crosses the barrier, but it can do so in both the blood-to-brain and brain-to-blood direction. Furthermore, the study showed that inflammation as triggered by lipopolysaccharide increased the uptake of α-syn by the brain. This is likely by disruption of the BBB itself, as it was confirmed in a later study that BBB leakage occurs early in the PD disease process.

α-syn is also found in the retina, specifically RPE cells, where it regulates dopamine production to some degree. Moreover, this protein is thought to function as a ferrireductase, an enzyme that reduces ferric (Fe$^{3+}$) iron to ferrous (Fe$^{2+}$). α-syn is regulated by iron and itself impacts iron levels. Iron has been found to accumulate in the substantia nigra in individuals with PD. Overabundance of iron causes the protein to accumulate and negatively impact the ability for both α-syn and dopamine function. An imbalance in this relationship causes a reduction in neuroretinal dopamine, which is thought to contribute to the visual manifestations of PD. RPE cells have the potential to offer therapeutic benefits when transplanted to the basal ganglia by producing adequate amounts of dopamine to replace the damaged dopaminergic neurons.

**PD and eye tracking**

Eye tracking is now being researched as another potential biomarker of PD. Interest in this stems from the fact that eye tracking is a non-invasive way to study the cognitive and neural processing of an individual in real time. Of the various ocular events that can be measured, saccadic eye movement has the greatest relevance to PD. Latency in saccades are found to be associated with the areas of the brain that are altered by the condition. Additionally, studies have used eye tracking to assess the therapeutic effects of PD medications. As a result, saccadic metrics are being considered as an objective means to diagnose and to monitor for progression of PD.

**What is the clinical syndrome known as “parkinsonism”? What are the differential diagnoses and how would you distinguish them from PD?**

The motor symptoms of PD are classic to the condition, but not solely associated with PD. Resting tremors, rigidity, shuffling gait and bradykinesia are part of the clinical syndrome known as “parkinsonism.” Other conditions can be associated with parkinsonism, including drug-induced parkinsonism, multiple system atrophy (MSA) and progressive supranuclear palsy (PSP) (Table 1). Drug-induced parkinsonism is commonly caused by antipsychotics. MSA and PSP can be differentiated from PD by how rapidly the condition progresses, with MSA and PSP known to cause a more rapid functional decline. Likewise, though falls are not uncommon in these conditions, those with PD typically do not experience falls as frequently until the middle to late stages of the disease process, whereas MSA and PSP may present with more frequent falls in the earlier stages. Another way to distinguish PD from MSA and PSP is the presence of visuoperceptual deficits, which are associated with the former rather than the latter. Additionally, dopaminergic treatment is more likely to improve symptoms from PD than from MSA and PSP. Furthermore, if the patient is noted to have dysfunction in vertical saccades, then PSP should be suspected.

**How should dry eyes be managed in patients with PD?**

Dry eye is a common problem in the general population, but is even more prevalent among those with PD and should be looked at differently with this group. A classical feature of PD is reduced blink rate, which leads to the characteristic “stare” in these patients and is thought to contribute to dry eyes. Dysfunction of the autonomic innervation to the lacrimal gland is also thought to contribute to reduced tear production. Individuals with PD should be evaluated for dry eyes and treated accordingly. When considering treatment with eye drops, such as artificial tears, it is important to assess the patient’s ability to instill the drops. Their motor impairment may prevent them from successfully doing so themselves. The provider should consider discussing if they have a caretaker who can help them administer the drops, or offer eye drop guides for those with relatively controlled tremor. Additionally, patients should be advised to be mindful about blinking more frequently because they tend to have a reduced blink rate.

**What are possible causes of diplopia in patients with PD and how can it be managed?**
The prevalence of diplopia in PD is not well-studied but is thought to be relatively common.\textsuperscript{29,47,48} Reported in up to 38% of patients with PD.\textsuperscript{29} Both central and peripheral pathways have been proposed as potential mechanisms.\textsuperscript{29} It may result from dysfunctional saccades and pursuit, a limitation on upgaze or, more frequently noted, convergence insufficiency (CI), which can affect the ability to read.\textsuperscript{7,8,48,49} In terms of management of CI, base-in prism in reading glasses may help as well as convergence exercises.\textsuperscript{6} When considering eyeglasses, bifocals and progressive lenses should be avoided.\textsuperscript{7} PD patients have a higher risk for falls than the general population. Furthermore, they tend to have a stooped posture, so it may be difficult for them to locate the correct area of their bifocals or progressive lenses to view through. This may increase their already high risk for falls. It is recommended to prescribe single-vision distance and near glasses with impact resistant materials for lenses, such as polycarbonate or Trivex. Additionally, if refraction yields large amounts of astigmatism, reducing it by its spherical equivalence would be of benefit for those with tremors because glasses may not be stable on them.\textsuperscript{7}

**How should glaucoma be managed in patients with PD?**

Though the pathophysiology is not clear, a correlation is found between PD and glaucoma. Older individuals with glaucoma are at increased risk for developing PD.\textsuperscript{50} Likewise, those with PD are at increased risk for developing glaucoma.\textsuperscript{51} They may develop primary open-angle glaucoma\textsuperscript{17} or angle-closure glaucoma, with the latter being more likely if the individual already has shallow anterior chambers, such as in the case of a high hyperope. Because patients with PD are taking dopaminergic medication, blockage of aqueous outflow can lead to angle closure.\textsuperscript{6} Management of glaucoma is the same as for the general population, although it is important to consider how PD patients’ tremors may affect monitoring with OCT and HVF and the ability to instill eye drops. If reliable test results are difficult to obtain, the patient may need to be monitored structurally. Again, one must consider discussing the availability of a caretaker to help administer drops, or offering an eye drop guide for those with relatively controlled tremoring. For patients unable to use eye drops, laser or surgical treatment options should be considered.

**How can contrast sensitivity loss or impairment in color vision be managed in patients with PD?**

The pathophysiology for contrast sensitivity loss and impairment in color vision is not well understood, but deficiency of retinal dopamine is suspected.\textsuperscript{5,7,15,19,26} In terms of management, some cases have shown improvement in both contrast and color vision with dopaminergic therapy for PD.\textsuperscript{5,6,19,24} This highlights the importance of co-managing these patients with their neurologist. An adjustment in medication may alleviate the impairment. For persistent contrast sensitivity loss, yellow filters can be prescribed to increase contrast. Furthermore, the patient should be advised to read and work with sufficient ambient light.\textsuperscript{7} Patients who still drive should be advised to limit their driving to the daytime.\textsuperscript{5,6}

**What should be considered if a patient with PD has visuospatial or visuoperceptual impairments?**

Visuospatial ability involves the processing of visual information about where objects are located relative to each other and oneself in the environment. Visuoperceptual function has to do with the recognition of objects. Impairment of both visuospatial and visuoperceptual functions can occur in PD. The impairments likely result from changes within the temporo-parietal cortex. Patients who still drive can be referred for a driving assessment. They can be trained in various driving skills, such as visual scanning.\textsuperscript{6,19,52}

**How should visual hallucinations be addressed in patients with PD?**

Visual hallucinations were originally thought to be a side effect of medications because dopamine may elicit them.\textsuperscript{3,7,8,19} Many drugs for PD are dopamine promoters of some form. More recent studies show that the reduced visual input to the occipital lobe causes an increase in activity being released. It is said that more than half of those with PD will at some point experience visual hallucinations, though this information is generally not reported voluntarily.\textsuperscript{51} Therefore, it is important to directly ask patients if they are experiencing this visual phenomenon. The under-reporting is thought to occur due to fear that others will think they are mentally unstable or perhaps not take them seriously.\textsuperscript{5,51} Patients should be reassured that it is not uncommon for someone with PD to have visual hallucinations, as it can be a side effect of the medications and/or the lack of visual input. Co-management with the neurologist for dosage or medication changes to assist the patient may be indicated.

**Conclusion**

Eyecare professionals have an important role to play in caring for the visual needs of patients with PD. These individuals have a higher prevalence of ocular symptoms that frequently interfere with daily activities compared with healthy age-matched individuals, as reported by Borm et al.\textsuperscript{28} Vision plays an even more critical role for patients with PD because visual guidance can help compensate for loss of motor control. This highlights the importance of addressing the visual needs of patients with PD. Because ocular motor dysfunction may improve with dopaminergic treatment, the authors recommend encouraging patients to take their medications on time.
Researchers are currently looking into retinal thinning and eye tracking as potential biomarkers for monitoring PD progression, assessing the effects of treatment and helping with earlier detection, before motor symptoms appear. While these areas of research are inspiring, a large, rigorous study to obtain conclusive findings has not yet been conducted. In the future, eyecare professionals may play a larger role in comanaging patients with PD given what is being researched now.

References


Bowen’s Disease of the Eyelid: a Teaching Case Report
Zainab A. Muhanna, OD, Angelina Tran, OD, FAAO, and Bhagya Segu, OD, MPH, FAAO | Optometric Education: Volume 47 Number 2 (Winter-Spring 2022)

Background

This case report reviews the clinical manifestation of Bowen’s disease (BD) in a patient who presented to the eye clinic with a chief complaint of a “bump” on his eyelid. BD (ICD-10: D09.22), also known as squamous cell carcinoma in situ, is a precancerous skin lesion confined to the epidermis. The etiology of this precancerous lesion includes sun and carcinogen (e.g., arsenic and occupational chemicals) exposure.1-3 The intent of this case report is to describe clinical characteristics of BD, appropriate workup, treatment, management and differential diagnosis. This report is intended for optometry students, optometrists and eyecare professionals.

Case Description

Initial visit: comprehensive eye exam

A 76-year-old Caucasian male presented to the eye clinic with a chief complaint of a “bump” on his left lower eyelid that he first noticed approximately 2 years prior. He reported the lesion had not grown in size but was cosmetically bothersome. The patient denied any associated bleeding, ulceration, pain or pruritus. This was a first-time occurrence of such a lesion on his eyelid; however, he reported a history of basal cell carcinoma (BCC), squamous cell carcinoma (SCC), actinic keratosis (AK) and seborrheic keratosis (SK). The BCC lesions were removed via excision from his right preauricular area and his left upper thigh. The SCC lesions were removed via excision from his left forehead. He had numerous AK lesions present on his left temple, left ear, forearms and hands, which were monitored annually by dermatology for progression. The SK lesion was removed from his right mid-chest via liquid nitrogen for cosmetic reasons.

The patient’s ocular and systemic history were significant for blepharitis, dry eye syndrome, a single episode of herpes zoster ophthalmicus of the left eye (which resolved in 2006), bilateral radial keratotomy (performed in 1989), bilateral age-related cataracts, prostate cancer (Gleason 6, diagnosed in 2010), and benign essential hypertension. His systemic medications included hydrochlorothiazide 25 mg tab and lisinopril 40 mg tab daily. The prostate cancer was being actively surveilled (most recent prostate specific antigen (PSA) level - 6.72 ng/ml; transrectal ultrasonography (TRUS) - 44.53 gm).

The presenting spectacle prescription was +1.50 +1.25 x025 in the right eye (OD) and +3.25 sph in the left eye (OS). Best spectacle-corrected visual acuities were 20/25 OD and 20/25 OS. Manifest refraction revealed no changes to the presenting spectacle prescription. Pupils were equal, round and reactive to light with no afferent pupillary defect noted. Extraocular motility and confrontation visual fields were normal in both eyes (OU).

A slit lamp biomicroscopy assessment of the anterior segment OU revealed meibomian gland dysfunction and trace blepharitis of the upper and lower eyelids. The upper and lower eyelids had normal apposition to the globe. The lower lid revealed a 1 mm x 1 mm scaly lesion at the infraorbital crease with no palpable lymph node suggestive of metastasis (Figure 1). Neovascularization, feeder vessels, telangiectasia, bleeding, ulceration and crusting were absent. Intraocular pressures were 10 mmHg OD and 11 mmHg OS, measured by Goldmann applanation tonometry. All other anterior segment findings were non-contributory. Dilated fundus examination revealed unremarkable optic nerves, vasculature, macula and peripheral retina OU. Based on the exam findings, the patient was referred to the oculoplastic department for further evaluation.

Referral to oculoplastics department: problem-focused eye exam

The patient presented to the oculoplastics department for lesion evaluation and biopsy. Evaluation of the lesion in maximum room illumination revealed a flat, reddish lesion with no apparent risk factors for metastasis and no palpable preauricular node. Upon slit lamp biomicroscopy assessment, the findings were confirmed from the initial comprehensive eye exam. Because the lesion did not appear ulcerated, crusted, pearly, or tan in color, the suspicion for BCC, SCC and SK were low. BD,
AK and psoriasis remained on the differentials to be ruled out. The patient was educated that the lesion could be monitored for change via photography, or a shave biopsy could be performed to give a definite diagnosis. The patient opted for biopsy of the lesion.

Risks, benefits and side effects were fully explained, and consent was obtained. The infraorbital crease was prepped with an alcohol swab and lidocaine. A blade was used to obtain a 0.6 cm x 0.3 cm skin shave excised to a depth of 0.1 cm and placed into a labeled container. Antibiotic ointment was placed on the surgical site, which was covered with gauze to allow for healing. The biopsy was sent to pathology for microscopic evaluation.

1 week post-biopsy: problem-focused eye exam

The shave biopsy of the lesion was positive for Bowen’s disease (BD). The patient was educated on the condition and given the option of topical treatment of the lesion with imiquimod for 6 weeks followed by a 3-month follow-up. The patient declined imiquimod treatment and preferred to pursue lesion excision. Risks and benefits were explained, and a wide-local excision was performed. A 1.3 cm x 1.1 cm tan-brown skin shave, excised to a depth of 0.2 cm, was collected and sent to pathology for evaluation. Slit lamp biomicroscopy assessment revealed complete excision of the lesion with an intact incision, 2+ ecchymosis and satisfactory lower lid position. The patient was prescribed erythromycin ethylsuccinate ophthalmic ointment to be used twice daily on the surgical site to assist with healing.

2-day postoperative evaluation: brief eye exam

The pathology microscopic examination was negative for malignancy of the surgical margins. A slit-lamp microscopic examination revealed satisfactory lower lid position with 2+ ecchymosis and 2+ edema. The lower lid incision was intact and healing well. The patient was instructed to continue erythromycin ointment twice daily for 1 week and to return for a 2-week post-op evaluation.

2-week postoperative evaluation: brief eye exam

At the follow-up visit, mild erythema was noted at the excision site, but it was healing well (Figure 2). The patient was directed to discontinue erythromycin ointment. The patient returned to the general optometry clinic and was to be followed as needed in the oculoplastic department. It was recommended that the patient have an eye examination at least once a year to monitor for any suspicious skin lesions.

**Educator’s Guide**

**Key concepts**

1. Characteristic traits of BD
2. Hallmark signs to differentiate malignant and benign skin lesions
3. Co-management and treatment – the optometric role in diagnosis of precancerous lesions
4. Prevention, care and patient education

**Learning objectives**

1. Identify ocular signs and symptoms of BD
2. Differentiate between BD and other precancerous and benign skin lesions
3. Describe various treatment approaches for precancerous skin lesions
4. Understand appropriate follow-up intervals and risk factors for precancerous lesion progression

**Discussion points**

1. Basic knowledge and concepts related to BD:
   a. Describe the classic presentation of a BD skin lesion
   b. Describe the etiology of BD and patient demographics
   c. Discuss risk factors involved in skin lesion progression
2. Differential diagnosis, prognosis, treatment and management:

a. What options are available to diagnose skin lesions, and which is most precise?
b. What is the prognosis of BD?
c. What are the treatment options, and which ones are expedient?
d. What is the recommended follow-up interval for patients who elect to monitor eyelid lesions?

3. Critical-thinking concepts:

a. The importance of optometry in the identification and co-management of skin lesions
b. Methods to help optometrists identify and properly describe eyelid lesions – terminology and high-risk characteristics to help with solidifying knowledge

Discussion

Teaching instructions and assessment methodology

This case report targets third- and fourth-year optometry students and optometry residents. Readers should study the entire background and case report and answer all discussion questions in the Education Guidelines. The images would be best highlighted in a PowerPoint presentation, as the presenter can ask students to describe the characteristics of the lesion. A verbal case discussion should also emphasize how malignant lesions can be very subtle in presentation, as with this patient.

The presenter should discuss the importance of:

1. obtaining thorough patient history (including questioning about known skin lesions or cancers)
2. evaluating eyelid architecture (both externally and with the slit lamp) to check for any lesions with asymmetry and irregular borders, changes in lid contour, redirection of eyelashes, madarosis or irregular skin texture
3. palpating and moving loose skin to reveal any abnormal characteristics such as elevation or firmness that can be hidden in the dermatochalasis of geriatric patients
4. photodocumenting and prompt referral for dermatological evaluation and biopsy

Pathophysiology

BD is referred to as carcinoma in situ, or “cancer in its place” in Latin, because abnormal cell growth remains confined to the epidermis (Figure 3) and is therefore considered precancerous. The epidermis is composed of three cell types: melanocytes, keratinocytes and basal cells. BD is a premalignant variation of keratinocytes, which are also referred to as squamous cells. Keratinocytes form at the bottom of the epidermis and rise to the top to be replaced (Figure 3). Progression of the lesion can lead to SCC, which occurs in 3-4% of cases. Approximately 5-10% of skin cancers occur on the eyelid, with SCC being the second most common eyelid malignancy. It accounts for approximately 5-10% of all malignant eyelid tumors.

Etiology, epidemiology and clinical presentation

The etiology of BD is multifactorial and it may arise spontaneously or from other precancerous lesions, such as AK. Chronic sun exposure, carcinogen (e.g., arsenic and occupational chemicals) exposure, human papillomavirus, previous injury to the skin, and immunosuppression have all been linked. BD is more prevalent in women and primarily affects individuals of Caucasian and Asian descent between the sixth and ninth decade of life. Early lesion formation is subtle and slow-growing, leading to a delay in diagnosis. Clinically, the lesions appear well-demarcated, dry and scaly as red patches or plaques. About 66% of the time, BD will appear as a single lesion. Lesions can vary in size and arise in areas with frequent sun exposure, such as the face, head and neck.

Evaluation and further testing

A comprehensive workup is necessary to diagnose an individual with BD. The lesion is examined for its color, shape, size,
border and elevation, and palpated to determine malignancy potential. Diagnosis is confirmed via biopsy or dermoscopy. A biopsy collects a tissue sample that is analyzed for the histological presence of a disease. BD biopsies are performed by shave, punch or excisional techniques. Shave biopsy is the preferred method and used for raised lesions that do not extend into the dermis. This procedure is cost-effective and has good cosmetic outcomes but is prone to inadequate sampling. Punch biopsies allow for full-thickness samples that require deeper tissue for diagnosis. Samples are limited to small areas (1-4 mm) and therefore also provide good cosmetic outcomes. Excisional biopsy removes an entire lesion or area of abnormality. Sutures are used to close the incision, which may leave a visible scar over time. Dermoscopy, or skin surface microscopy, is a non-invasive method to evaluate the epidermis and detect diagnostic patterns that are suggestive of malignant or benign lesions. BD lesions are typically clustered together and have glomerular and dotted vessels when evaluated with dermoscopy.8,9

**Differential diagnosis**

SK, AK, psoriasis, superficial BCC and cutaneous SCC must be ruled out in cases of suspected BD (Table 1). SK lesions are a benign proliferation of the epithelium arising on the face of elderly individuals and are pigmented, raised lesions with fissures, giving them a ‘stuck-on’ appearance.10 These lesions are easily removed and do not have malignant tendencies. AK is also a squamous cell carcinoma in situ but differs from BD in its appearance.11 AK lesions are smaller pink, red or brown patches that cluster in areas of chronic ultraviolet (UV) exposure.5,10,11 They are frequently treated with liquid nitrogen or topical antineoplastic agents. Psoriasis is an inflammatory reaction of the skin in which cells multiply quickly and build on themselves. Psoriasis is differentiated from BD by its thick, silvery scales that overlie a pink patch of skin covering areas of the scalp and joints. Psoriasis is incurable but can be controlled with retinoids, topical steroids or phototherapy. BCC appears as raised, pearly-white nodules with telangiectasia. BCC represents about 90% of eyelid malignancies and presents in middle-age, fair-skinned individuals.3,5 BCC histologically differs from BD in that it arises from basal cell transformation within the epidermis.10 Most BCC lesions are found on the neck and head, but approximately 20% are periorcular, with the lower eyelid being the most frequent periorcular location.2,3,6 BCC is locally invasive, rarely metastasizes, and is removed via surgical intervention or topical antineoplastic agents. SCC is the second most common eyelid malignancy, and like BCC, is typically found on the lower eyelid.3,8,12 SCC arises from small keratin patches that transform into an ulcerated lesion with irregular borders.10,12 These lesions are invasive and metastasize through the lymphatic system, surrounding tissue and organs.3 SCC is commonly treated via surgical excision or radiation therapy.

**BD treatment and management**

Several treatment options for BD are available and categorized into surgical and topical interventions. Surgical interventions include excision, Mohs micrographic surgery, cryotherapy and curettage and desiccation (C&D). Frozen section-guided wide-local excision is the simplest and most utilized surgical intervention; it involves removing the lesion along with a quarter inch of the surrounding tissue.13 The mass is subsequently sent to pathology for frozen section examination to ensure that all margins are cancer-free. Mohs micrographic surgery provides a high cure rate and is used when tissue sparing is vital as is the case for larger lesions with irregular borders; however, it is more expensive than traditional excision.7,13 C&D is one of the most cost-effective treatment options and is performed under local anesthesia; the skin lesion is scraped away and cautery is used to prevent hemorrhaging.13 Cryotherapy involves the use of liquid nitrogen to destroy skin cells.13 Liquid nitrogen freezes a lesion causing it to scab and fall off. Of all the surgical techniques, wide-local excision is the treatment of choice for BD.13

Topical interventions include photodynamic therapy (PDT) and antineoplastic agents. With PDT, a cream specific to cancer cells is applied to a lesion and exposed to laser, releasing toxic material thereby destroying abnormal cells.13 Antineoplastic agents are medications used to treat cancer by inhibiting cell division. Two specific antineoplastic medications used in BD are imiquimod and 5-fluorouracil. Imiquimod stimulates the immune system and is thought to increase the presence of lymphocytes, macrophages and dendritic cells within a BD lesion.2,13,14 5-fluorouracil interferes with DNA synthesis to reduce

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**Table 1. Click to enlarge**

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Microscopic Features</th>
<th>Differentiation</th>
<th>Treatment</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>BD</td>
<td>Basaloid cells</td>
<td>Differentiated</td>
<td>Reduced</td>
<td></td>
</tr>
<tr>
<td>SK</td>
<td>Multinucleated cells</td>
<td>Differentiated</td>
<td>Reduced</td>
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<tr>
<td>AK</td>
<td>Hyperkeratosis</td>
<td>Differentiated</td>
<td>Reduced</td>
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</tr>
<tr>
<td>Psoriasis</td>
<td>Inflamed epidermis</td>
<td>Differentiated</td>
<td>Reduced</td>
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<td>BCC</td>
<td>Well-differentiated</td>
<td>Differentiated</td>
<td>Reduced</td>
<td></td>
</tr>
<tr>
<td>SCC</td>
<td>Squamous cell</td>
<td>Differentiated</td>
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Sources: Bath-metal et al; Merta et al; Gomdik et al; Balsubramaniam et al; Rathi et al; Prav-Mohania et al; Rankouji et al.
cell proliferation and has a cure rate of about 80%.  

**Prognosis and patient counseling/prevention**

Overall, BD has a favorable prognosis with a risk of conversion to SCC of 3-4%. After treatment, there is a 10% chance of BD reoccurrence. Optometrists should counsel their patients on preventative measures including the use of broad-spectrum sunscreen, wide-brimmed hats, UV400 sunglasses, avoiding chronic sun exposure, refraining from tanning bed use, and actively self-examining their skin for new or developing lesions. Patients should be educated on abnormal characteristics of a lesion such as sclerosis, hemorrhaging, allodynia, growth and/or change in pigmentation. Patients with a history of skin cancer should also have a screening with their primary care physician or dermatologist every 6-12 months.

**Critical-thinking concepts**

Eyecare providers can actively assess for sun damage on a patient’s face and detect associated lesions that are at risk for progression. Malignant lesions tend to change over time, whereas benign lesions appear stable at follow-up exams. Some key features to keep in mind for malignant lesions are they tend to be firm to the touch, have irregular borders, are asymmetric in appearance, and may distort eyelid margins. When assessing and documenting a lesion’s appearance, the clinician should start with maximum room illumination and observe the lesion at arm’s length. Note should be made of color, orientation, approximate size and any distortion to the eye anatomy caused by the lesion. Slit-lamp magnification should be used to observe any vessel growth, ulceration, hemorrhaging or discharge. Photography of a lesion is recommended to monitor for any changes at subsequent exams.

**Conclusion**

BD is a precancerous lesion that may have delayed diagnosis due to its slow-growing nature. Lesions frequently arise between the sixth and ninth decade of life on areas of sun-exposed skin. Co-management between eyecare professionals and dermatologists is imperative to successfully diagnose and treat BD as well as monitor patients for recurrence. BD appears similar to other skin lesions and thus requires biopsy for a definitive diagnosis. Lesions are typically treated surgically with excision but can also be managed topically with antineoplastic agents. BD has a favorable prognosis with a low risk of progression to SCC.

**References**

Understanding Geographic Atrophy in Advanced Non-Exudative Age-Related Macular Degeneration: a Teaching Case Report

James Rogala, OD, FAAO | Optometric Education: Volume 47 Number 2 (Winter-Spring 2022)

PDF of Article

Background

Age-related macular degeneration (AMD) is a common condition which, as the name implies, results in acquired degenerative changes involving the macular region of the eye. The initial presentation is typically the focal deposition of abnormal amounts of extracellular debris, known as drusen, within and around Bruch’s membrane, the acellular layer separating the retinal pigment epithelium (RPE) from the choriocapillaris. As drusen accumulate, the normal exchange of nutrients and metabolic waste products between photoreceptors and their underlying vascular supply may become impaired, resulting in gradually progressive bilateral vision dysfunction. Eventually, RPE cell death may ensue and lead to focal atrophy of overlying photoreceptors and the underlying choriocapillaris. The resultant sharply demarcated atrophic patches at the posterior pole are referred to as geographic atrophy (GA). These atrophic areas usually first appear in the perifoveal region and may slowly expand to include the fovea itself, producing severe central vision loss due to what is considered the end-stage of “non-exudative” AMD. In some instances, choroidal neovascularization (CNV) may develop and be accompanied by leakage and the accumulation of extracellular fluid, which often causes abrupt vision loss due to what is termed “exudative” AMD.1,2

AMD is a multifactorial disorder with a multitude of genetic, environmental, and nutritional components contributing to its development. The main risk factor by far is age, and the condition is almost by definition non-existent in those under the age of 50.3 Demographically, Caucasians are affected more often than those of other ethnicities. Positive family history and certain genetic profiles also predispose individuals to the development of AMD. The major modifiable risk factor is cigarette smoking.4 AMD has consistently been found to be a leading cause of severe irreversible vision loss in developed countries throughout the world.5,6,7 Unfortunately, there is currently no treatment for the non-exudative form, which constitutes up to 90% of all cases of AMD.1,2 Nonetheless, optometrists can benefit these patients by reducing their risk of progression, detecting treatable exudative manifestations, and providing vision rehabilitation. Clinical trials, which may enable treatment in the near future, are under way.

The following case report is intended to help facilitate discussion and understanding of key concepts related to the clinical presentation and management of GA amongst optometry students, residents and practitioners.

Case Description

A 91-year-old Caucasian gentleman presented for examination as advised by his primary care physician. He was accompanied by his daughter who provided a history of long-standing vision loss, described 5 years earlier as “legal blindness” due to “macular degeneration,” with no recent changes. She also reported that he had undergone cataract surgery on both eyes several years ago and that a metallic foreign body was removed from his left eye many years ago. His most recent eye exam had been “a few” years prior with an ophthalmologist. His most recent eye exam had been “a few” years prior with an ophthalmologist. The daughter further explained that her father had not seen the ophthalmologist since then because his other health concerns had taken precedence and his vision had not seemed to change. Family ocular health was uncertain, but it sounded as if he may have had siblings (brother and sister) who also experienced vision loss from macular degeneration in their later years. His daughter reported that he was being treated for “heart disease,” diabetes, hypertension and high-cholesterol, and that he had undergone multiple cardiac bypass surgeries. A list of current medications was obtained that was consistent with and appropriate for the conditions described. The
patient was being visited weekly at his home by a nurse practitioner to ensure adequate management of the aforementioned cardiovascular conditions, with periodic office visits to the primary care provider who had advised ocular examination.

Best-corrected visual acuity was 20/200 in each eye at distance and near with a prescription of OD: +0.50 -0.50 x 100, OS: +0.75 -0.75 x 105 using a +3.50 near add. Due to difficulty with fixation, cover test results were undeterminable, but extraocular muscles were unrestricted. Color vision testing using Ishihara plates was unreliable. Pupils were equal, round and reactive to light with no relative afferent pupillary defect. Confrontation visual fields were full to finger counting OU, while Amsler grid testing revealed central scotomas in each eye. Intraocular pressures were measured as OD: 13 mmHg, OS: 14 mmHg via non-contact tonometry after applanation tonometry was deemed unsafe/impractical due to excessive head movement and blinking. Slit lamp examination revealed normal lids and lashes, quiet conjunctiva, and corneas that were clear centrally with mild arcus OU. There was no significant staining of conjunctiva or cornea with fluorescein in either eye, and both anterior chambers were deep and quiet with clear, well-positioned posterior chamber intraocular lenses in each eye. Von Herrick estimation of both anterior chamber angles was 4/4. The patient’s pupils were dilated with 1% tropicamide OU. Posterior segment evaluation revealed well-circumscribed areas of chorioretinal atrophy centrally in both eyes (Figure 1). Optic nerves were well-perfused with minimal cupping, distinct margins and temporal peripapillary atrophy OU. Retinal vasculature was essentially normal apart from trace dot and blot hemorrhages with very mild arteriole narrowing and arteriovenous crossing changes at the posterior pole of each eye (Table 1).

A diagnosis of advanced non-exudative AMD resulting in central GA was made based on the history obtained from the patient’s daughter and the distinct fundus appearance at presentation. Given the stable nature of the patient’s condition and lack of any currently proven treatment to reverse his vision loss, the patient and his daughter were reassured that he would not completely lose sight from this disorder and informed of the potential for low vision services to maximize his remaining vision. Following this discussion, both the patient and his daughter expressed a desire to pursue a low vision consultation as suggested, and appropriate referral was made in-house to a trusted optometric colleague with residency training and experience in low vision rehabilitation. In addition, they were advised to continue home monitoring with the Amsler grid and to return for a comprehensive eye examination in 12 months, or sooner if any changes were noticed. In discussion with the patient’s daughter, more frequent follow-up was deemed unnecessary at this time given the apparent stability of his condition and the difficulties of traveling to the clinic in addition to attending to his other healthcare needs.

Summary of low vision consultation

The patient was seen a month later for a comprehensive vision rehabilitation evaluation. Our low vision specialist noted that he was hoping for help with reading his bible, bird-watching and gardening. There were no significant changes in history, medications or findings from the comprehensive eye examination conducted a month previously. A tritan color vision defect was detected with D-15 testing (tested OU) and a moderate decline in contrast sensitivity OU was elicited using the Mars letter chart. The patient and his daughter were provided with extensive counseling on the nature and extent of his vision loss and numerous vision aid devices were trialed. From among those demonstrated, the Eschenbach Magno 8x Binoculars were found to be especially useful and information was provided on how to obtain a loaner with the potential for purchase. He was also provided with a completed application for the state’s audiobook library. Finally, they were informed that he qualified for legal blindness status and they were referred to the appropriate state agency to obtain services for independent living. Prior to being discharged, they were advised to contact low vision services if they had problems using any of the devices or services offered by them and to follow up with me as directed.

Education Guidelines

The target audience for this case report as a learning exercise would primarily be optometry students or residents. Specifically,
this case could serve as a teaching/learning tool within a didactic course on posterior segment disease because the focus is on medical management and the disease process. It would not be appropriate for a low vision course (though a case report on AMD emphasizing that aspect of care certainly could be).

This particular case could also be presented in a clinical grand rounds format to supplement direct patient care activities as part of a clinical rotation or externship. In fact, during the early months of the COVID-19 pandemic we used cases such as this for that very purpose while our students were prohibited from participating in direct patient care. While this case was not used in that manner, those that were effectively bridged the gap in patient care activities during the months that was not possible.

A final way in which this type of case report can be integrated into the curriculum is as a remediation or make-up assignment. For example, I am considering employing it in this manner within our posterior segment disease course when examination results indicate an individual requires additional instruction (outside the class as a whole) to achieve an acceptable level of competency on this topic. In this role, the student could be provided with the case report as a self-directed learning exercise. After allowing sufficient time for review, assessment might entail having the student answer the discussion questions presented below. In this context, the literature suggests this would perhaps best assess critical thinking and clinical decision-making via an oral or short-answer examination (as opposed to multiple-choice questioning).

### Learning objectives

After reviewing this case report and subsequent discussion, one should be able to:

1. Appreciate the burden imposed by AMD and GA on society and individual patients
2. Understand the pathophysiology behind AMD and GA
3. Differentiate AMD and GA from similar-appearing disorders
4. Understand the utility of various ancillary tests and when each is indicated
5. Appropriately counsel and manage patients presenting with AMD and GA

### Key concepts

1. The epidemiology, demographics and morbidity associated with AMD and GA
2. The underlying pathophysiology of AMD and GA
3. The differential diagnoses of AMD and GA
4. The utility of ancillary testing in the diagnosis and management of AMD and GA
5. Proper management of patients with various manifestations of AMD and GA

### Discussion questions

1. Discuss how problematic AMD and GA are on both a population and individual level:
   a. what is the incidence/prevalence?
   b. what are the main risk factors, in terms of age, ethnicity and environmental influences?
   c. what are the consequences in terms of vision, overall well-being, cost?

2. Discuss the pathophysiology of AMD and GA:
   a. which anatomical structures are involved and how does this alter ocular function?
   b. what detrimental changes occur at the biochemical, cellular and histological level?
   c. what is the typical progression of non-exudative AMD from onset through end stage?

3. Discuss how optometrists diagnose AMD and GA:
   a. what is the relationship between drusen and AMD?
   b. what other disorders display drusen and/or chorioretinal atrophy?
   c. how can an optometrist distinguish between AMD/GA and conditions that look similar?

4. Discuss the clinical tools available to help diagnose and manage AMD and GA:
   a. what different types of imaging facilitate diagnosis and management? How?
   b. what non-imaging tests (labs, etc.) are useful? How?
   c. how is progression monitored in and out of the office?
5. Discuss the current standard of care and what the future holds for managing AMD and GA:

a. what is the appropriate optometric management of each stage of AMD?
b. what is the role of nutrition supplementation at each stage of AMD?
c. when should an optometrist refer a patient with AMD? To whom? For what?

Teaching and assessment methodology

The purpose of this case report is to provide a real-world example of AMD with GA that can be used as a platform for discussion to increase understanding and improve patient care. Educators may choose to present only the case findings initially and provide the discussion questions as homework, to be completed individually or in groups, reserving further discussion for a subsequent meeting. Alternatively, the entire case report, including the discussion section, could be assigned as a self-directed individual or group study assignment.

Assessment may be formative (reviewing discussion question answers together with feedback) or summative (to evaluate proficiency). For the latter, the instructor might wish to create multiple-choice or short-answer questions based on the discussion questions provided. In either case, the goal should be to ensure competency, critical thinking and the ability to apply the concepts discussed to diverse clinical scenarios.

Discussion

Age-related macular degeneration remains the most common cause of severe irreversible vision loss in developed countries such as the United States and Canada.\(^1\) It is conventionally designated as being either the “dry” non-exudative form or the “wet” exudative form. While the advent of anti-vascular endothelial growth factor (anti-VEGF) medications has enabled treatment and, for some, reversal of vision loss in those with exudative AMD, there is currently no proven treatment for the more common non-exudative form of AMD.\(^2\) This is significant because more than a million Americans are afflicted with GA.\(^3\)

Visual impairment due to AMD is a substantial societal burden. Various epidemiological studies have found the non-exudative manifestation of the disorder, for which there is no current treatment, to account for approximately 90% of all AMD cases.\(^1\) Unfortunately, demographic trends mean the incidence of both forms of AMD is increasing and expected to rise dramatically in the coming years. Within the United States, the number of individuals with AMD increased from 1.75 million to 2.07 million between 2000 and 2010, an increase of 18%, and that number is projected to more than double to 5.44 million by 2050.\(^4\) In terms of healthcare costs, the World Health Organization estimated the direct costs of vision impairment due to AMD in the United States, Canada and Cuba alone (WHO subregion AMR-A) at nearly $100 billion (in 2008 USD).\(^5\) Thus, given the magnitude of the problem, it is imperative that practicing optometrists understand this disorder and keep abreast of the latest developments in diagnosis and management in order to properly care for this large and growing patient population.

While the pathogenesis of AMD is complex and multifactorial, certain risk factors have been recognized. Age is the most significant, with those over age 75 being three times more likely to develop the disorder compared to their cohorts age 65-74.\(^6,7\) Genetic factors are another important risk factor and probably help account for the fact that AMD is more prevalent in Whites than in Blacks while prevalence in the Hispanic and Chinese populations falls somewhere in between.\(^8,9\) Specific genes have been shown to either predispose or be protective for AMD development, most notably the complement factor H (CFH) gene.\(^10\) Several environmental and lifestyle factors have also been investigated. Smoking has been identified as the main modifiable risk, roughly tripling the likelihood of developing AMD compared to non-smokers and increasing the risk of progression in those with AMD.\(^2,10,11\) Moreover, the combination of genetic and environmental risk factors, such as smoking, appears to have a synergistic effect on the progression of AMD.\(^12\) It is also likely that obesity, poor diet and cardiovascular disorders such as hypertension are risk factors though to what extent remains unclear.\(^13\) It is less certain whether other proposed factors, such as UV exposure, pose a significant risk.\(^14\)

The complex pathogenesis of AMD means there is still much to be learned and a detailed discussion is well beyond the scope of this case report. Nonetheless, an examination of basic principles enables a better understanding of current and future management strategies. First, it is important to realize that some of the initial changes seen in AMD are not unique to this disorder and may even be considered part of the normal aging process. For example, drusen are neither pathognomonic (they occur in other conditions such as Doyne honeycomb retinal dystrophy and certain kidney disorders) nor necessarily pathological (small drusen are a common occurrence in healthy elderly patients who retain normal vision function).\(^13\) It is only when there is an abnormal accumulation of drusen not due to other pathological processes but brought about by the interplay of various factors that predispose certain individuals to AMD, that we can label it as their cause.Second, it is important to realize that there is no single cause of AMD. Oxidative stress, activation of the complement immune pathway, and inflammation are among the many biochemical processes that have been implicated in initiating and propagating AMD.\(^15\) What is clear, is that AMD does not simply result from the space-occupying effect of drusenoid material. Research has shown that not only is
the retinal architecture above drusen abnormal in AMD patients, but these effects extend beyond the borders of drusen into neighboring drusen-free areas of the retina. This demonstrates that the underlying disease mechanism is not simply mechanical distortion of retinal tissues. Thus, it should be understood that it is an intricate interaction of multiple risk factors that is responsible for initiating and propagating the various changes that result in AMD.

The clinical presentation of non-exudative AMD is initially indicated by the abnormal accumulation of drusen within the macula, seen upon fundus examination as discrete yellow-white lesions, which may coalesce over time, becoming confluent. Pigmentary disruption within the RPE may ensue and is observed as a mottling of the normal fundus appearance with hyper- and hypopigmentation. This may eventually develop into frank loss of RPE and subsequently the overlying photoreceptors that depend on it, leading to discrete areas of chorioretinal atrophy within the macula referred to as GA. These typically have fairly distinct borders within which the underlying choroidal vasculature may be visible. All of these changes tend to occur bilaterally, though there may be asymmetry, and progress gradually over months to years. Should exudative AMD develop, one may observe the appearance of hemorrhages, exudates or pigment epithelial detachments.1,2,13

In terms of symptoms, patients usually first notice difficulty in dim light as rod dysfunction predominates in the early stages.27,28 Metamorphopsia may become noticeable when there is significant derangement of photoreceptor alignment brought about by progressive underlying accumulation of drusenoid material. Finally, if areas of GA develop, they will be associated with dense/absolute scotoma. Fortunately, these patients typically retain some level of ambulatory vision even with severe bilateral central GA because the peripheral retina is not affected. As with fundus changes, the symptoms of non-exudative AMD typically progress slowly and bilaterally over months or years. Should conversion to the exudative form of AMD occur, patients may notice a sudden unilateral decrease in vision.1,2,13

The diagnosis of AMD relies heavily on clinical examination. As previously mentioned, the appearance of significant macular drusen in a patient of at least 50 years of age that are not attributable to any other disorder is a hallmark finding. Optical coherence tomography (OCT), fundus autofluorescence (FAF) and multimodal imaging may all be used to distinguish and quantify drusen.29-32 These same tools may also be used to distinguish GA in late-stage non-exudative AMD from disciform scarring, which often results from exudative AMD and may look similar to inexperienced clinicians; the former being a loss of tissue (atrophy) while the latter represents additional (scar) tissue. Thus, macular OCT scans display thinning with GA, fluid (intra-retinal, subretinal or sub-RPE) during active exudative AMD, and fibrotic tissue (which is hyper-reflective) with disciform scar formation. FAF also plays a prominent role in assessing GA in late-stage non-exudative AMD, because any hyperfluorescence adjacent to areas of atrophy (which appear hypofluorescent) signals a likelihood of progressive enlargement of the area of atrophy.32 The use of fluorescein angiography is typically reserved for detecting or confirming exudative AMD, and recent studies have shown that spectral domain OCT may be sufficient for that purpose in many cases.33

For the specific case being presented, these differential diagnoses were initially considered:

- non-exudative AMD with central GA
- exudative AMD with disciform scarring
- a long-standing macular dystrophy (such as areolar macular dystrophy)
- end-stage retinal toxicity (such as hydroxychloroquine retinopathy)

Key characteristics for each of these disorders are outlined below, followed by a summary of the clinical reasoning used to arrive at the correct diagnosis in this patient’s case.

- Non-exudative AMD typically presents after age 50 with drusen and RPE changes affecting the macula of both eyes. Drusen and pigmentary changes typically increase gradually over years and may eventually result in confluent central photoreceptor and RPE loss described clinically as GA.
- Exudative AMD occurs when CNV causes leakage and/or hemorrhage within the macula. These changes and their resultant vision symptoms may appear rather abruptly and often eventually result in the deposition of scar tissue.
- Macular dystrophies usually manifest early in life as bilateral vision and fundus changes that may progress to frank chorioretinal atrophy over time. Family history often reveals the inheritance pattern of the genetic disorder responsible for the macular changes.
- Retinal toxicity may occur bilaterally following exposure to certain medications, etc. The timeline separating introduction of a specific causative substance and the particular nature of subsequent anatomic and functional abnormalities affecting the maculae are keys to the diagnosis.

As noted earlier, we diagnosed our patient with advanced non-exudative AMD resulting in central GA based on the history obtained from the patient’s daughter and the distinct fundus appearance at presentation. The fact that his vision problems began only after age 50, along with the absence of a known family history of ocular dystrophy or vision problems before middle
age in any of his relatives, made any form of macular dystrophy (such as areolar macular dystrophy, which may eventually produce a similar appearance) unlikely. Similarly, a thorough review of the patient’s medication and social history failed to elicit a known exposure to any potentially toxic substances that could have been responsible for his macular changes. Though he had been diagnosed with some type of macular degeneration by a previous provider, the fact that his vision loss progressed slowly and symmetrically in both eyes over many years made it highly unlikely that our patient experienced the exudative form of AMD. Thus, the diagnosis of non-exudative AMD with central GA OU was fairly straightforward in this case.

Although there is currently no proven treatment for the non-exudative form of AMD, optometrists can help these patients in a number of ways. The ground-breaking Age-Related Eye Disease Study (AREDS) and subsequent AREDS2 have shown that using specific high-dose multivitamin and mineral supplements is effective in reducing the risk of progression to advanced AMD for those with at least moderate AMD in either eye. The formulation derived from AREDS2 (the exact mechanism of action, which includes antioxidative effects, is still being teased out) is as follows:

- 500 mg vitamin C
- 400 IU vitamin E
- 10 mg lutein
- 2 mg zeaxanthin
- 80 mg zinc
- 2 mg copper

At present, the determination as to what constitutes “moderate” AMD is made by counting the number and size of individual drusen deposits as viewed through the pupil, a process that is tedious and prone to inaccuracies. Recent studies have shown reduced retinal thickness (an indication of cellular pathology) above drusen is linearly proportional to drusen height, but only modestly correlated with drusen width. This suggests that current criteria used to classify AMD severity and guide treatment decisions based on drusen diameter may need to be refined. The practical implication is that by considering drusen height and/or volume (as measured non-invasively via OCT), we may be able to improve the protocol used clinically to determine which patients are likely to benefit from AREDS2 supplements to decrease the rate of progression to advanced AMD. This could potentially lead to substantial decreases in the number of AMD patients who suffer severe vision loss. In terms of prevention, it is also imperative that clinicians counsel patients about modifiable risk factors, such as cigarette smoking, that may exacerbate their condition and direct them toward the appropriate resources (smoking cessation programs, etc.) in order to implement beneficial behavioral changes when applicable.

The ability to detect conversion from non-exudative AMD to the exudative form is extremely important because FDA-approved treatments such as anti-VEGF injections are most effective when implemented earlier. Home monitoring with a simple Amsler grid has traditionally been used between periodic office visits for this purpose. However, newer devices such as the ForeseeHome AMD Monitoring System (Notal Vision), which assess preferential hyperacuity perimetry and employ telemonitoring, appear to be superior in this regard. There have even been smartphone applications developed that may be used in place of the Amsler grid.

Unfortunately, while it is possible to slow the progression of non-exudative AMD and treat those cases that convert to the exudative form of AMD, there is no effective treatment for non-exudative AMD at present. However, studies are currently investigating a number of potential therapies. For example, several studies have looked into intravitreal injections of complement inhibitors as a potential therapeutic intervention to treat or prevent GA. In particular, a recently concluded phase 2 trial of C3 inhibition with pegcetacoplan (which interrupts an early step in the biochemical pathway leading to activation of the complement pathway thought to contribute to the progression of GA) resulted in statistically significant reductions in the growth of GA lesion area compared with sham treatment and demonstrated acceptable safety to proceed to phase 3 studies. Multiple orally administered medications are also being investigated for their potential to reduce the expansion of GA. One of these is the TOGA clinical study to evaluate treatment with Oracea (doxycycline 40 mg), which began in 2013 and was originally scheduled for completion in December 2020 until being delayed by the COVID-19 pandemic. This derivative of tetracycline has been shown to have anti-inflammatory and other inhibitory properties that it is hoped may limit GA progression. Given the similarities in pathogenesis between AMD and atherosclerosis, statin medications commonly prescribed to treat high cholesterol and triglyceride levels have been looked at as a means of reducing the incidence and/or progression of non-exudative AMD. One such pilot study of 23 patients concluded that 80 mg daily of atorvastatin (Lipitor) may reduce drusen deposits and improve VA in a subgroup of patients with AMD. Other studies, however, have had mixed results and the role of statins in the treatment of AMD remains uncertain. Perhaps most interesting, human trials of stem cell therapy involving the transplantation of RPE cells derived from human embryonic stem cells to treat GA have begun. However, most experts expect the commercial application of stem cell therapy to be at least a decade away, and doctors should warn patients to avoid predatory clinics offering stem cell treatments that are not FDA-approved. Despite such practices, initial results from legitimate research have been promising and stem cell therapy may one day prove to be an effective treatment.
option for our patients. Additional potential medical therapies not mentioned in this discussion are currently being investigated as possible treatments for non-exudative AMD.

Although no form of surgery has been developed to treat non-exudative AMD, there is a viable FDA-approved surgical procedure that has proven beneficial as a low vision aid. This involves removing the crystalline lens and replacing it with a miniature telescope that enlarges and projects images from the central visual field onto functioning areas of retina in those with severe central vision loss due to GA. Specifically, the telescope is used in one eye of patients with bilateral central vision loss to enable them to see some of what normally would have been lost from their central visual field, while leaving the other eye unaltered to conserve peripheral vision. Prior to undergoing the procedure, patients must demonstrate improvement in visual acuity during a trial period with an external telescope. While this has been shown to benefit certain patients with bilateral central vision loss from non-exudative AMD, our patient was unfortunately not a candidate because he had previously undergone cataract surgery OU, which is a contraindication for the procedure. However, a clinical trial investigating the safety and efficacy of the telescopic implant in post-cataract surgery patients is currently under way, so this could become an option for him in the future.

Given the current lack of an effective treatment for central GA due to advanced non-exudative AMD, low vision services are an extremely important aspect of patient management. A thorough discussion of the entire spectrum of low vision devices and services available to these patients is beyond the scope of this case report. However, it is essential that every optometrist appreciate that such services exist and understand how to access them for our patients. This is an area in which optometry is at the forefront, and intra-professional referrals to an appropriately trained low vision specialist can often substantially benefit these patients by enabling them to best utilize their remaining vision, increase independence, and thereby dramatically improve their overall quality of life.

Conclusion

This case illustrates the clinical presentation of central GA in advanced non-exudative AMD and outlines the most effective management strategies currently available, while exploring potential interventions that may provide improved outcomes in the future. While the diagnosis is usually fairly straightforward, as in this case, we as clinicians have no approved or effective treatment to offer our patients at the present time. Thus, prevention is an important aspect of management and all optometrists must be vigilant in identifying at-risk patients (those with early or intermediate non-exudative AMD), counseling them to reduce/eliminate modifiable risk factors such as smoking, recommending AREDS2 supplements when appropriate, and ensuring proper surveillance in order to detect and refer conversion to the exudative form as soon as possible (when anti-VEGF therapy is most effective).

For those patients who, despite our best efforts, develop central GA, low vision services are an essential component of management. Not every optometrist needs to be a low vision specialist; however, we must all recognize when such services are indicated and ensure our patients receive them. Ongoing research continues to shed light on the pathophysiology of this common, all too often visually devastating condition, and provide the promise of novel therapeutic options in the not too distant future. Therefore, optometrists must keep up with the latest advances in order to give their patients hope, but not false hope, and be positioned to direct them toward approved clinical trials for which they may be eligible when appropriate.

References

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The Many Faces of Polypoidal Choroidal Vasculopathy: a Teaching Case Report
Ansu M. Abraham, OD, FAAO, Shephali Patel, OD, MS FAAO, and Danielle Kalberer, OD FAAO | Optometric Education: Volume 47 Number 2 (Winter-Spring 2022)

PDF of Article

Background

Polypoidal choroidal vasculopathy (PCV) is characterized by subretinal, vascular lesions associated with serous and hemorrhagic detachments of the retinal pigment epithelium (RPE). Typically, it presents as massive (greater than 4 disc diameters) subretinal hemorrhage or orange nodules in the macular area. It can also occur in the peripapillary and extramacular areas, albeit less often. Other names given to this condition include “posterior uveal syndrome” and “multiple recurrent RPE detachment in black women.” It is a variation of choroidal neovascular membrane (CNV); however, it has a different pathophysiology than CNV related to exudative age-related macular degeneration (AMD) associated with subretinal hemorrhage.

PCV starts unilaterally but may later develop in the fellow eye. While it can be diagnosed in patients as young as 20 years, patients usually become symptomatic between age 50 and 65. There is no definite male or female predilection; however, initial reports mentioned higher prevalence in middle-age women than in men, with an approximately 4.7:1 ratio. Other studies from Japan report PCV is more common in Asian men than women. It is more common in pigmented individuals including Blacks, Asians and Hispanics. It may be present in 4%-10% of Caucasians with presumed AMD depending on the study, and in 23.9%-54.7% of Asian patients with presumed AMD. Other risk factors for PCV have been identified as smoking, cardiovascular disease, hypertension and hyperlipidemia (similar to those of AMD). High body mass index also has been identified as a risk factor.

While macular PCV is often misdiagnosed as exudative AMD or central serous choroidopathy, their pathophysiology and treatment differ. Multimodal imaging is often necessary to distinguish between similarly appearing conditions. This teaching case report discusses a patient with PCV in the peripapillary area that was previously diagnosed as multiple other conditions. It presents the pathophysiology, retinal manifestations and most current diagnosis and evidence-based management guidelines for PCV. The target audience is optometry residents and third- and fourth-year optometry students.

Case Description

A 55-year-old African American male presented for his annual eye exam with no visual or ocular complaints. Medical history included remission of prostate cancer and longstanding headaches around his occipital lobe, which were monitored by a neurologist without treatment. Ocular history included pseudophakia of both eyes and an amelanotic lesion in the peripapillary area of the left eye. Family ocular history was unremarkable.

The retinal lesion of the left eye had been diagnosed as a retinal hamartoma 2 years prior by a retinal specialist. One year after that diagnosis, the lesion had grown and begun to hemorrhage. The retinal specialist then re-diagnosed the lesion as a retinal cavernous hemangioma and administered one injection of intravitreal bevacizumab (Avastin) at a standard dose of 1.25 mg in the left eye.

At the current visit, the patient’s best-corrected visual acuity (BCVA) was 20/20 in each eye. Pupils reacted normally, ocular motilities were full in each eye and confrontation visual fields were full in each eye. Ocular motilities were full. Intraocular pressure with Goldmann applanation tonometry was 14 mmHg in the right eye and 15 mmHg in the left. Slit lamp exam was unremarkable and posterior chamber intraocular lenses were clear and centered in each eye.

Dilated fundus exam revealed an amelanotic lesion in the peripapillary area of the left eye with two associated hemorrhages: one was located superior-temporal and one superior-nasal. On photographic review, it seemed the lesion had grown. The right eye’s fundus evaluation was unremarkable. Cirrus optical coherence tomography (OCT) at the area of the lesion revealed the presence of enlarged pachyvessels with subretinal fluid. More advanced OCT imaging was not available at the facility.

Given the patient’s history of headaches and the growing lesion (now associated with retinal hemorrhaging), magnetic
resonance imaging of the brain and orbits was ordered to rule out a space-occupying lesion. The results were normal. The patient was also referred to an ocular oncologist who ordered indocyanine green angiography (ICGA) and fluorescein angiography (FA) to properly diagnose the condition. ICGA revealed focal hyperfluorescent “polyps” during the early phase and leakage from “polyps” during the late phase, which was instrumental in the diagnosis (Figure 5).

The patient was diagnosed with PCV in the left eye based on the fundoscopic and angiographic findings. The ocular oncologist recommended photodynamic therapy (PDT) alone or in combination with anti-vascular endothelial growth factor (VEGF) treatment in the future if the vision were to become affected. Fortunately, the lesion and the hemorrhages regressed with monitoring alone at the subsequent 3- and 6-month follow-up visits (Figure 6). The retina specialist continued to monitor the patient without treatment.

Figure 1. Amelanotic lesion in the peripapillary region of left eye was identified 2 years prior and diagnosed as retinal hamartoma. Click to enlarge

Figure 2. 1 year after the first diagnosis, the lesion was re-diagnosed as retinal cavernous hemangioma. Click to enlarge

Figure 3. Apparent lesion growth and associated hemorrhaging observed at the current visit warranted referral to ocular oncology, which eventually led to a PCV diagnosis. Click to enlarge

Figure 5. A) Early-phase ICGA shows focal polyps. B) Late-phase ICGA shows leakage from polyps. Click to enlarge

Figure 6. The regressed PCV lesion at the 3-month follow-up visit. Click to enlarge

Education Guidelines

This case report is appropriate for discussion among third- and fourth-year optometry students and would be most applicable to those in primary care or ocular disease rotations. The authors recommend presenting the case as a PowerPoint with concurrent verbal discussion. A slide presentation is ideal for step-by-step case review with graphics and ancillary test results. A parallel verbal discussion of the case report should incorporate Table 1 and Figure 7 as teaching tools. Table 1 aids in teaching proper classification and description of PCV lesions. Figure 7 is a tool for teaching PCV treatment and management recommendations. The verbal discussion should also include the discussion questions (below) to evaluate the learning objectives and student understanding of the condition, its management and treatment. The discussion questions should be completed once the case and discussion section of the paper have been thoroughly read and reviewed.

Key concepts
1. Identify demographics and epidemiology of PCV
2. Identify clinical presentation of PCV
3. Consider appropriate differential diagnoses
4. Review pachychoroid classification of retinal disease
5. Determine appropriate referral and treatment recommendations

Learning objectives

1. Identify the various types and clinical manifestations of PCV
2. Understand the ocular anatomy of the condition along with its classification on the pachychoroid spectrum
3. Identify testing needed to confirm the PCV diagnosis, specifically OCT, FA and ICGA
4. Understand how the recommended treatment correlates with the pathophysiology

Discussion questions

1. What clinical signs and patient symptoms would be expected in a case of PCV?
2. What additional testing would assist in the diagnosis of PCV?
3. What are the typical features of this condition on OCT, FA and ICGA?
4. What newer multimodal imaging features assist in diagnosis of PCV? How do they differentiate PCV from similar-appearing conditions such as exudative AMD?
5. What specialty referrals would you consider making if you suspect PCV? What is the role of the optometrist in co-managing this condition with a specialist(s)?
6. What is the current evidence-based treatment for PCV?
7. What is the prognosis for PCV?
8. What factors can influence the recurrence of PCV lesions after PDT?

Discussion

PCV was first described by Yannuzzi as peculiar polypoidal, subretinal, vascular lesions associated with serous and hemorrhagic detachments of the RPE in the macula.1 Yuzawa reported two distinct subtypes of PCV. The first type has both feeder and draining vessels, also known as branching vascular network (BVN). The second type has few inter-connecting channels but no BVN. The former is termed polypoidal choroidal CNV; the latter is termed typical PCV. He described polypoidal CNV as a deformation of the CNV under the RPE. In contrast, typical PCV without BVN is characterized by hyalinized arteriolosclerosis of choroidal vessels. Vitrectomy of a typical PCV eye shows massive exudative change in blood plasma and basement membrane-like deposits of slight granulomatous tissue beneath Bruch’s membrane.4

Genetic studies have linked subtypes of PCV to particular genes. Complement factor H and age-related maculopathy susceptibility (ARMDS2) gene is seen in Japanese and Caucasian patients with polypoidal CNV, but not in typical PCV.4 Both these genes are strongly associated with exudative AMD.4,14,15 Tanaka and associates suggested complement component-2 and complement factor B gene variants might be possible genetic markers for polypoidal CNV, but not typical PCV.16 These genes are known activators of alternative complement cascade in Caucasian patients with AMD. Despite these genetic similarities between AMD and PCV, differences in susceptibility patterns have been identified and can aid in proper diagnosis.17

Studies have also reported an upregulation of VEGF and pigment epithelial derived factor in the aqueous humor of eyes with PCV.18,19 This change might be responsible for the neovascular complexes seen in PCV. These factors are prominent in active CNV and less common in new vessels where fibrosis or quiescent CNV was prominent.17

On dilated fundus exam, the dilated inner choroidal vessels of a PCV lesion appear as multiple reddish-orange nodules beneath the RPE.20 According to Tan, there is a predilection for the macular region at 87.5%, and less frequent presence in the peripapillary region (6.5%) and extramacular region (5.6%). In the aforenoted study, macular region was defined as within 2 disc diameters (or 3 mm) from the center of the fovea. Peripapillary region was defined as within 1 disc diameter from the optic disc margin. Extramacular region was considered anywhere outside the peripapillary and macular region. PCV lesions can be single and isolated or widespread and multiple.21
It is not uncommon to see spontaneous massive subretinal hemorrhages due to the rupture of the thin-walled choroidal vessels. Hence, PCV lesions can also be classified clinically as quiescent, exudative or hemorrhagic. Quiescent is when there are polyps but no subretinal or intraretinal fluid or hemorrhage. Exudative is when there are no hemorrhages but some exudative changes such as sensory retinal thickening, neurosensory detachments, pigment epithelium detachment (PED) and subretinal lipid exudation. Hemorrhagic is defined as any subretinal or sub-RPE hemorrhage with or without other exudative changes.

PCV has been categorized as part of the pachychoroid spectrum of retinal conditions. This group of conditions, in addition to PCV, includes central serous chorioretinopathy, pachychoroidal pigment epitheliopathy and pachychoroid neovasculopathy. Pachychoroid refers to a thickening of the choroid with characteristic pathogenic dilation of blood vessels in Haller’s layer. These vessels are referred to as “pachyvessels” and are associated with an abnormal increase in choroidal permeability. Additionally, these pachyvessels are often accompanied by thinning of the choriocapillaris and middle choroidal layer vessels that overlie them. These features help to distinguish PCV from similarly appearing exudative AMD cases because the choroidal thickening pattern typical of pachychoroid is not associated with exudative AMD. In addition, there are minimal to no drusen associated with PCV, and there are often drusen associated with AMD.

**Diagnostic testing**

OCT is a valuable, non-invasive imaging modality appropriate in PCV cases. On OCT, PCV lesions appear as chronic multiple “serosanguineous” detachments of the RPE and/or neurosensory retina. Sato and associates observed a classic appearance of a “double layer sign” seen in 59% of eyes with PCV on OCT. It is seen as two highly reflective lines, one in the RPE and the other in the Bruch’s membrane. It signifies the location of the BVN or choroidal vascular network. According to the Asia-Pacific Ocular Imaging Society PCV Workgroup, a combination of three specific OCT findings supports a diagnosis of PCV: sub-RPE “ring-like” lesions, en face complexes of RPE elevation, and sharp-peaked PEDs. The ring-like lesions appear as round structures underneath PEDs with varying levels of reflectivity; the en face RPE complexes appear as multiple PEDs connected by a hyper-reflective vascular network; and the sharp-peaked PEDs appear as “thumb-like” protrusions with steep vertical inclines. When using these three findings as diagnostic criteria, an accuracy level higher than 80% was achieved.

The advancements in OCT technology have allowed for enhanced depth (ED) analysis of the choroid. The pathognomonic polypoidal lesions of PCV have been more specifically localized to a space between the RPE and Bruch’s membrane. ED-OCT has been used to identify features that distinguish PCV from exudative AMD. The presence of increased choroidal thickness in eyes with PCV vs. those with AMD suggests different pathologies. Swept source OCT (SS-OCT) of pachychoroid patients has demonstrated that there is not always choroidal thickening; some patients classified as pachychoroid may have normal or even decreased choroid thickness due to concurrent atrophy of choroidal vasculature. SS-OCT also demonstrated that the area of maximal choroidal thickness in pachychoroid patients does correspond to the area with the greatest concentration of pachyvessels even if that maximum thickness level is not very high.

OCT angiography (OCTA) is also useful in PCV diagnosis. A study by Chan et al. evaluated 31 patients with a total of 72 PCV lesions confirmed with ICGA. It was found that all lesions identified by ICGA were consistently identifiable on OCTA. Additionally, 53 of 72 lesions showed “cluster-like” structures on en face imaging of the relevant layers, and 50 of 72 demonstrated “internal channels of flow” on cross-sectional imaging. The larger the lesion was, the more likely it was to have the aforesaid OCTA appearance. Srour also found that branching vascular networks could be reliably identified using this non-invasive imaging modality. When OCTA was used to classify features of BVN, three main patterns emerged. A trunk-like pattern was most frequently observed, in about half of cases, followed by a “glomeruli-like” vascular network and a “stick” pattern.

On FA, a quiescent PCV lesion typically has some occult CNV characteristics with early hyper- and hypofluorescence. Exudative lesions are observed as progressive and uniform hypofluorescence in the early phase with intense pooling in the late phase. Hemorrhagic lesions are hypofluorescent secondary to blockage of dye by blood. Hence, macular PCV is often

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**Table 1. Click to enlarge**

<table>
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<tr>
<th>Location</th>
<th>Clinically</th>
<th>FA/ICGA/OCTA Findings</th>
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<tr>
<td>Panretinal</td>
<td>Quiescent</td>
<td>Typical PCV</td>
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<tr>
<td>Macular</td>
<td>Exudative</td>
<td>Polypoidal CNV</td>
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<td>Extramacular</td>
<td>Hemorrhagic</td>
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PCV = polypoidal choroidal vasculopathy; FA = fluorescein angiography; ICGA = indocyanine green angiography; OCTA = optical coherence tomography angiography; ONV = choroidal neovascularization.

Sources: Yutani et al., Koh et al., Tan et al., Koh et al.
ICGA is the gold standard for diagnosing, classifying and treating PCV. Indocyanine green absorbs and emits near-infrared light and is therefore able to penetrate RPE deeper. The dye also has a higher binding affinity to plasma protein, so it does not leak as rapidly from the choriocapillaris as fluorescein. ICGA should be considered whenever ophthalmic examination reveals spontaneous, massive subretinal hemorrhage, notches or hemorrhagic or serous PED, a lack of response to anti-VEGF therapy, and/or clinically visible orange-red subretinal nodules. However, appearance of orange-red nodular elevations is not diagnostic for PCV because small PEDs without polyps can have a similar appearance.

In early- to mid-phase ICGA, larger choroidal vessels fill with dye while the surrounding area remains hypofluorescent. The “polyps” in terminal vessels, aneurysmal dilations, become hyperfluorescent prior to the retinal vessels. Leakage from the “polyps” begins during the mid phase. During this phase, the size of the choroidal hyperfluorescence matches the clinical observation of the lesion. During the late phase, the previously surrounding darker areas become hyperfluorescent while the center of the lesion becomes hypofluorescent. In the very late phase, a non-leaking PCV lesion will become “washed-out,” but a leaking PCV lesion remains hyperfluorescent.

According to evidence-based guidelines for diagnosis of PCV by Tan, PCV is defined as single or multiple focal nodular areas of hyperfluorescence from choroidal circulation within 6 minutes after injection of indocyanine green with one or more of the following features (statistics in parenthesis represent prevalence of the relative factor):

- nodular appearance on stereoscopic view of ICGA (95.3%)
- hyperfluorescent halo surrounding the focal hypofluorescence (81.3%)
- association with BVN on ICGA (77.6%)
- pulsatile filling of the polyps in dynamic ICGA (25.2%)
- focal hyperfluorescence corresponding in location to an orange nodule of fundus (37.4%)
- association with massive (> 4 disc diameters) submacular hemorrhage (7.5%)

Multiple reports have also suggested that pulsatile hyperfluorescent filling of the polyp nodule might be unique to PCV.

**Treatment/management**

Treatment of PCV is based on location of active leakage and whether it is affecting vision. 50% of lesions are self-limiting and not visually significant. PCV is considered active if any of the following are present: ophthalmic findings, OCT and/or angiography that attributes PCV to a drop in vision of at least 5 letters (on ETDRS chart), subretinal fluid with or without intraretinal fluid, PED or subretinal hemorrhage, or angiographic evidence of leakage. 60% of active lesions will have complete resolution of serous retinal detachment when laser photocoagulation is applied to ICGA-identified polypoidal feeder vessels. Therefore, active extrafoveal exudative leakage should be treated with laser photocoagulation. Active subfoveal and juxtafoveal PCV lesions are considered sight-threatening and should be treated based on the guidelines established by the EVEREST, EVEREST II and PLANET studies.

The EVEREST study was a multicenter, double-masked, prospective study investigating symptomatic PCV cases treated with verteporfin PDT combined with ranibizumab (Lucentis) vs. PDT alone vs. ranibizumab monotherapy. At 6 months, 71.8% of patients had complete regression with verteporfin PDT treatment alone with BCVA improvement of 7.5 letters, whereas 77.8% had complete regression with PDT verteporfin combined with ranibizumab with a 10.9 letter improvement. Ranibizumab monotherapy had a complete regression rate of 28.6% and improvement of 9.2 letters. Based on EVEREST findings, subfoveal and juxtafoveal PCV should be treated either with ICGA-guided verteporfin PDT or a combination of verteporfin PDT and three 0.5-mg ranibizumab intravitreal injections at monthly intervals. The results proposed that combination therapy should be considered the treatment of choice in the following scenarios: leakage from BVN and polyps, large amounts of subretinal fluid or exudation associated with PED, ICGA features that are ambiguous between PCV and CNV, and/or if the lesions are a combination of typical PCV and typical CNV. Ranibizumab monotherapy is suggested for initial therapy if verteporfin PDT treatment is contraindicated or not possible. Subfoveal and juxtafoveal PCV should be monitored 3 months after initial treatment using FA, OCT and ICGA. If there is still leakage on FA/OCT but complete polyp regression on ICGA after 3 months, retreatment with ranibizumab is recommended. If there is incomplete regression of
polyps, retreatment with verteporfin PDT monotherapy combined with ranibizumab alone is recommended.\textsuperscript{22}

The follow-up study, EVEREST II, investigated the safety and efficacy of ranibizumab monotherapy vs. combination therapy with ranibizumab and PDT in treating PCV. Participants were randomized into one of two treatment groups, ranibizumab plus PDT or ranibizumab with sham PDT, and monitored for 24 months. The average BCVA improvement in the combination therapy group was 9.6 letters as compared to the monotherapy group improvement of 5.5 letters. 56.6\% of polyp lesions had complete regression in the combination therapy group as compared to 26.7\% in the monotherapy group (which was consistent with findings in EVEREST). The results suggest that combination therapy with ranibizumab and PDT remains the superior treatment option over ranibizumab monotherapy.\textsuperscript{37}

The PLANET study investigated the safety and efficacy of aflibercept (Eylea), with and without PDT in treatment of PCV. All patients received treatment with intravitreal aflibercept for the first 3 months, then were randomized into an aflibercept monotherapy group or a group qualifying for “rescue” PDT, which was subdivided into a sham PDT group and a rescue PDT group. After 52 weeks, mean improvement in BCVA for the aflibercept monotherapy group was comparable to the aflibercept plus PDT rescue group at 10.7 vs. 9.1 letters respectively. The proportion of patients with polyp regression after treatment was also comparable in the two groups with 33.1\% regressed after aflibercept monotherapy and 29.1\% regressed in the aflibercept plus rescue PDT group. This study concluded that aflibercept monotherapy was at least as effective for most PCV patients as combination therapy and additional treatment with rescue PDT did not offer a significant benefit.\textsuperscript{38}

It has been noted that presence of a BVN tends to offer a less efficacious response to PDT as compared to lesions without BVN because of increased likelihood of recurrence. BVNs tend to leak even if the polyps themselves have completely regressed with PDT treatment. Hence, polypoidal CNV tends to have poorer prognosis for visual outcomes.\textsuperscript{22}

The case at hand can be evaluated using the adapted evidence-based guidelines in Figure 7 and the OCT features discussed above. Fundoscopic features of orange-red subretinal nodules along with spontaneous subretinal hemorrhage were present along with OCT features of pachyvessels and subretinal fluid. ICGA identified focal filling of polyps along with hypofluorescence matching the orange nodules seen on retinal exam. The level of leakage and its impact on vision were considered to determine treatment. Fortunately for this patient, the lesion was located near the optic nerve rather than at or near the macula and therefore close monitoring was the management of choice.

Conclusion

PCV is a commonly misdiagnosed condition. Guidelines for its management differ from those of similar-appearing conditions such as exudative AMD; therefore, initial proper diagnosis provides patients with the best opportunity for successful treatment. PCV is also a condition that can spontaneously regress or recur (if it has an associated BVN). This relapsing-remitting nature of PCV makes management challenging. Most often, PCV can be monitored. However, if the lesion is visually significant, ICGA-guided PDT with verteporfin in combination with anti-VEGF treatment should be utilized until the lesion has regressed. The presence of BVNs increases recurrence rate and decreases prognosis of polypoidal CNV compared to typical PCV. It is important for optometrists to understand the pathophysiology and progression of PCV to properly diagnose the condition, coordinate specialist referrals and counsel patients on prognosis. Such understanding also provides optometrists with increased ability to co-manage PCV patients undergoing treatment or monitor patients in whom treatment is not indicated. Lastly, this provides an opportunity for optometrists to provide rehabilitative and low vision services if the condition becomes visually significant enough to impede a patient’s activities of daily living.

References


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