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You're the flight surgeon at a Midwestern Air Force base when a 33-yr-old, male Caucasian C-17 loadmaster presents with painless, decreased vision in his right eye. He was seen the prior week for an upper respiratory infection (URI), which was treated symptomatically with Mucinex and ibuprofen. Today he notes the onset of visual blurring/clouding and decreased central vision on the right, on awakening. He denies headache, diplopia, pain with ocular movement, speech difficulty, vertigo, dizziness, numbness, weakness, or incoordination. He is otherwise healthy and denies prior similar occurrences. He has a waiver for reflux disease and is on maintenance therapy with Prilosec. He is also dyslipidemic, currently controlled with Zocor. He has no other significant past medical history or history of ophthalmological surgery. Review of systems is noncontributory, except as noted above, and some minor residua from his URI several days earlier. His vitals are within normal limits and he is obese, with a body mass index of 31. Through a combination of your examination and your local optometry office, you determine that the patient has decreased central visual acuity and color vision oculus dexter (OD), relative afferent pupillary defect OD, and optic nerve swelling OD. His intraocular tensions, as measured by applanation, were 14 mmHg bilaterally.

1. What is your initial diagnosis, based on these findings?

A. Central retinal vein occlusion.
B. Optic disc (nerve head) drusen.
C. (Atypical) optic neuritis.
D. Ocular histoplasmosis syndrome.

ANSWER/DISCUSSION

1. C. Optic neuritis (ON) is a clinical diagnosis based on history and physical examination findings. It is a demyelinating disorder of the optic nerve that typically presents as acute, painful, monocular vision loss.[1] Common visual deficits include visual field defects, color vision deficits, and reduced visual acuity. In 15–20% of patients subsequently diagnosed with multiple sclerosis (MS), ON is the presenting diagnosis and occurs in one-half to two-thirds of MS patients during the course of their illness.[20] Central retinal vein occlusion (CRVO) is the second most common retinal vascular disorder and a significant cause of vision loss. Although it usually occurs over age 50, younger patients can develop it as well.[18,19] CRVO is most often associated with compression of a retinal vein by an adjacent atherosclerotic retinal artery, which ultimately causes increased vascular permeability and leakage of fluid into the surrounding retinal tissue.[4,6,24] In this case, there were no hemorrhages or venous dilation demonstrated on fundoscopic exam, decreasing the possibility that this was CRVO. Optic disc drusen (ODD) are congenital and developmental anomalies of the optic nerve head commonly seen as an incidental finding during routine eye exams. ODD tend to lie beneath the surface of the optic nerve head, but may become visible later in life as yellow-white refractile bodies, always found superficial to the lamina cribrosa. ODD typically demonstrate elevation and blurring of disc margins.[2,8,13] Since the patient's optic nerve head did not demonstrate any yellow-white refractile bodies or disc margin blurring, the diagnosis of ODD is extremely unlikely. Ocular histoplasmosis syndrome

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(OHS) is the most common form of ocular disease caused by *H. capsulatum*. In the United States, OHS is an important cause of loss of central visual acuity among adults less than 60 yr of age. Most patients are diagnosed between 20 and 50 yr of age with a median age of 36. The highest prevalence occurs along the Ohio and Mississippi River valleys, where up to 80 million people are at risk of developing the condition.[14,17] The diagnosis of OHS is clinical and made via fundoscopic examination, with typical lesions appearing as small, atrophic, "punched-out" chorioretinal scars or "histo spots" in the midperiphery and posterior pole of the eye. These were not identified on fundoscopic examination, essentially ruling out this condition.

2. What about this case makes the ON "atypical"?

A. His age.
B. His race.
C. His gender.
D. His pain level.

ANSWER/DISCUSSION

2. D. Recall that the patient presented with a lack of ocular pain, whereas typical ON demonstrates pain with ocular movement. ON onset generally occurs between 18 and 49 yr of age[3,10] and has an incidence up to 5 per 100,000, most commonly in northern latitudes (the United States and Northern Europe).[20] Diagnosis occurs more often in Caucasian-Americans than African-Americans and may occur more often in women than men. Atypical presentation involves African-American race, age < 16 yr old, age > 45 yr old, bilateral simultaneous ON, lack of ocular pain (with eye movement), lack of improvement within 4 to 6 wk from symptom onset, progressive loss of visual function beyond 2 wk after onset of symptoms, or the presence of retinal hemorrhages, cotton-wool spots, or macular exudates.[1]

You call the patient back into your office to discuss the findings. After further questioning he admits that in addition to waking up this morning with decreased vision, he has noticed some recent, temporary decreases in vision OD while exercising, particularly on hot days. This persists for about 30 min post-exertion.

3. What is the name of this interesting phenomenon?

A. Uhthoff phenomenon.
B. Pulfrich phenomenon.
C. Entoptic phenomenon.
D. Extinction phenomenon.

ANSWER/DISCUSSION

3. A. Uhthoff phenomenon is a temporary blurring of vision that occurs when there is an increase in body temperature in patients with MS, ON, and other optic neuropathies. The symptom may also occur as a result of emotional stress, menstruation, increased illumination, or even a hot shower. Uhthoff phenomenon is a common observation among U.S. Air Force aircrew with ON. Military operational extremes characterized by increased heat exposure, such as desert operations or hot, closed cockpit/crew stations, may place military personnel at an increased risk for Uhthoff-related functional impairments.[11] Pulfrich phenomenon refers to altered perception of moving objects and is also associated with ON. Entoptic phenomenon pertains to transient formations or "floaters" in the visual field. Extinction phenomenon is a condition in which individual stimuli placed in the visual field are seen, but when the nasal field of one eye and the temporal field of the other eye are stimulated simultaneously, the subject fails to see one of the stimuli. This condition is most commonly seen following a parietal lobe stroke.

You send the loadmaster for further evaluation by neurology, ophthalmology, and ultimately neuro-ophthalmology. Two different brain magnetic resonance imaging (MRI) studies, 3 mo apart, revealed no central demyelinating lesions, but there was persistent pan-sinusitis, which earned him a referral to otolaryngology. Cervical MRIs revealed no demyelinating disease, but did show degenerative cervical disease at multiple levels. Visual evoked potentials showed delayed P-100 waves OD, which is consistent with ON. A lumbar puncture (LP) was performed for cerebrospinal fluid analysis, but was not analyzed due to improper specimen refrigeration. He experienced post-LP headaches for several days afterwards and declined another LP. The headaches resolved spontaneously and did not require additional treatment.

Your original diagnosis is confirmed by the experts: atypical ON OD, possibly post-infectious in etiology, with clinical residua of visual field loss and Uhthoff phenomenon. You look at the current Medical Standards Directory and are not surprised that ON is a disqualifying diagnosis for a loadmaster.* You then open up the Air Force Waiver Guide, noticing that trained, Flying Class (FC) III Airmen with two negative MRIs 3 mo apart and no definite MS can be waived by their major command.[5] Cerebrospinal fluid analysis is typically warranted when the initial MRI is negative for demyelinating lesions, but you'll explain the LP debacle in the waiver. You are not busy, so you decide to start writing the aeromedical summary (AMS), also ensuring that you have ordered all the appropriate studies.

4. Which of the following is NOT specifically required for an initial waiver for ON?

A. Neurology consultation.
B. Visual evoked potentials.
C. Threshold visual field studies.
D. Optical coherence tomography.

ANSWER/DISCUSSION

4. B. Visual evoked potentials can aid in the diagnosis of ON or MS, but are not specifically required for an initial ON waiver. The AMS for an initial ON waiver should include a full discussion of all clinical diagnoses requiring a waiver, a complete discussion of the patient's history of ON, consultation from ophthalmology and neurology, and threshold visual field studies at initial diagnosis and 3 mo later.

* U.S. Air Force. Section C: eyes and vision USAF medical standards, C49. In: Medical standards directory. 2014:10. [Accessed 18 Oct. 2014]. Available from https://kx2.afms.mil/kj/kx4/FlightMedicine/Documents/Medical%20Standards%20Directory%20(MSD)/Approved%20MSD%206%20October%202014.pdf to those with access.

Moreover, LP results, if clinically indicated by a neurologist, including oligoclonal band and myelin basic protein analysis, are required. Finally, the AMS should include a discussion of the patient's brain MRIs at initial presentation and 3 mo later, as well as optical coherence tomography,[5] which is used to identify decreases in the retinal nerve fiber layer, a finding that is suspicious for axonal loss.[12,22,23]

The disqualified loadmaster was ultimately sent to the Aeromedical Consultation Service (ACS) to be evaluated for an FC III waiver recommendation. At presentation he stated that his visual symptoms had improved, but he still noted some visual blurring with exertion that typically resolved within 20 min. This was confirmed at the ACS, where a treadmill-induced elevation in his body temperature revealed a marked loss of visual acuity OD. His vision went from 20/20 pre-exercise to 20/100 post-exercise and did not improve for 15 min. He was otherwise asymptomatic and further ophthalmological testing revealed no other disqualifying diagnoses. Your otolaryngology referral from several months ago confirmed the pan-sinusitis and he was being considered for sinus surgery.

AEROMEDICAL DISPOSITION

Since ON typically manifests during the span that makes up the most active years of an aircrew member's career and also increases the risk of developing MS, the diagnosis can have profound implications on future career performance and longevity. In a study of 31 military aircrew who developed ON between 1963 and 1994, with follow-up ranging from 7 to 30 yr, 39% went on to subsequently develop MS.[11] ON is disqualifying for FC I/IA, II, IIU, and III. It is not specifically listed as disqualifying for air traffic controller/ground-based controller (ATC/GBC) and missile operator duty (MOD) personnel, but MS is for all classes. If the ON is visually symptomatic, it would then be disqualifying for ATC/GBC and MOD duties. An Aeromedical Information Management Waiver Tracking System search in November 2014 revealed a total of 44 cases with the diagnosis of ON; 21 (48%) were disqualified, most typically due to the development of MS. There were no FC I/IA cases, 21 FC II cases with 12 disqualifications, 22 FC III cases with 9 disqualifications, 1 MOD case with no disqualification (although the AMS stated the member had MS), and no ATC/GBC cases (Van Syoc D. Personal communication; 2014).

The current U.S. Army Flight Surgeon's Aeromedical Checklists state that a waiver for ON may be considered, provided MS has been definitively excluded and the patient has recovered and is clinically stable with normal visual acuity, stereopsis, and color vision.[25] The U.S. Navy Aeromedical Reference and Waiver Guide discusses ON under the topics of MS, color vision abnormalities, and decreased visual acuity, but no separate heading for ON exists.[15] The Federal Aviation Administration requires cases of ON for all classes of pilots to be referred to them for disposition and reviews these cases individually after receiving a Report of Eye Evaluation from the aviation medical examiner.[7]

The primary aeromedical concerns for this aviator with atypical ON are variable decreases in visual performance that are often unpredictable by either exam or imaging study. He also has an increased future risk of developing MS. The risk of relapse from typical ON with normal MRI findings is low, as evidenced by the Optic Neuritis Treatment Trial, and is considered aeromedically acceptable. Likewise, data from the same trial indicate that the risk of developing MS in patients with a normal brain MRI is about 22% over 10 yr and 25% over 15 yr,[16] which is also felt to be aeromedically acceptable. Nevertheless, 1 study of 81 patients with ON suggests that those with symptoms of vision change associated with exertion could indicate a higher risk of recurrent ON or developing MS.[21]

In addition, the patient's initial symptoms were temporally associated with an acute URI, raising the possibility that his ON may be related to an infectious etiology. Two different MRIs revealed significant bilateral disease in multiple paranasal sinuses. There have been rare reports of vision loss secondary to ON in the presence of chronic sinusitis that was not associated with any symptoms of acute orbital cellulitis, although the pathogenesis of vision loss in these reports is not known. However, it is theorized that possible mechanisms could include a reactive ON or optic nerve vasculitis secondary to adjacent inflammatory sinus disease.[9]

A final, significant aeromedical concern in this case is the substantial loss of visual acuity demonstrated via treadmill testing at the ACS. Fortunately, the patient's vision returned to his pre-exercise state with normalization of his body temperature, as is typical with Uhthoff phenomenon. It is possible that this loss of vision could be induced by duties typical for a C-17 loadmaster, especially in the setting of a hot desert environment. This could be exacerbated by altitude-induced hypoxia. Such a loss of vision would be associated with a sudden loss of stereopsis and thus inability to effectively scan or judge the position of objects in and around the aircraft. This could pose a significant risk to himself, the crew, and the mission should it occur, particularly during a critical phase of flight. Therefore, an FC III waiver was unfortunately not recommended.

The patient returned to the ACS 1 yr later and reported a marked improvement in his symptoms, most notably after undergoing sinus surgery several months prior. All of his new testing was benign and, significantly, no objective decline in his visual acuity was demonstrated on provocative treadmill testing. This time an FC III waiver was recommended, valid for 2 yr. He should continue annual neuro-ophthalmological consultation and brain MRI studies to look for early pathological changes, especially those associated with MS.

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