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Optic Disc Drusen Resulting in Disqualifying Field Loss

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Optic Disc Drusen Resulting in Disqualifying Field Loss

Abstract

Background: Optic nerve (or disc) drusen is the presence of hyaline bodies at the optic nerve head. The drusen may be visible upon funduscopic examination or may present as buried. Timely diagnosis and responsible imaging may help inform the patient of the potential for future concerns. The long-term prognosis is good for most patients, however, they may experience progressive peripheral vision loss that may reduce the patient's quality of life. Neuroprotective options have previously been discussed with minimal clinical effectiveness, however, new medications may aid in future treatment.

Case Report: A patient presenting with mild and slowly progressing vision loss was examined and found to have optic disc drusen. Visual fields were done to quantify the extent of vision loss and revealed the patient no longer met the criteria for his commercial driver's license. Findings, imaging, and treatment options are discussed.

Conclusion: While no effective treatments exist currently, the potential benefit of brimonidine as a neuroprotective agent is discussed along with other future potential options. An assessment of the viability of the patient's cost benefit ratio is discussed.

Keywords

Optic nerve drusen, optic disc drusen, ODD, non-glaucomatous visual field loss, neuroprotection, neuroimaging, commercial driver's license (CDL)

Cover Page Footnote

Acknowledgements: I'd like to thank my family for their patience and support.

INTRODUCTION

Optic disc drusen exist as superficial or buried hyaline material within the optic nerve, anterior to the lamina cribrosa, and often present bilaterally. The inheritance pattern is autosomal dominant. The presence of optic disc drusen may be associated with retinitis pigmentosa, Alagille syndrome, or pseudoxanthoma elasticum.[1] In most patients there are no associated ocular or systemic conditions. A variety of imaging options are available to aid the clinician in the diagnosis. With increasing age, the patient may experience an associated decrease in vision.[1]

CASE REPORT

A 60-year-old African American male presented on October 1, 2015 to the eye clinic due to complaints of decreased vision in the right eye. He noted that his vision had slowly (over the course of "several months") decreased. He reported that his vision varied throughout the day and that he was unable to improve his vision by adjusting his glasses. He denied any change in the vision in the left eye. His visual acuity with correction was OD 20/40-2 (pinhole no improvement) and OS 20/20. His habitual spectacle prescription was +1.50-1.75x160 OD and +1.75-1.25x020 OS /+2.50. He had undergone cataract removal in his right eye 3 years prior. He denied using any ocular medications.

His systemic history was positive for hypertension, arthritis and kidney disease. He reported taking: Exforge HCT® 10-320-25 mg, Metoprolol Succinate ER, Tekturna HCT 300-25 mg, Furosemide 80mg, Klor-Con, Spironolactone 25 mg, Uroxatral 10 mg, Aspirin 81 mg, Vitamin D-3 5000 IU, Cranberry 84 mg, Alpha Lipoic Acid 200 mg, Fish Oil 1000mg/ 300mg omega-3, and Flaxseed oil 1300 mg. He had no known drug allergies and denied smoking or drinking. He was orientated to person, place and time.

The patient's pupils were equally round and reactive to light and accommodation. Extraocular motilities had full range of motion in both eyes. Confrontation visual fields were full to finger counting in both eyes. Intraocular pressures were 15 mm Hg in the right eye and 16 mm Hg in the left eye with Goldman applanation tonometry at 10:51 AM. A biomicroscopic exam revealed trace injection on the bulbar conjunctiva of both eyes. The adnexa was unremarkable in the right and left eyes, with normal lids and lashes. The corneas were clear, irises were brown, anterior chamber was without cells or flare, angles were open by Van Herick to 4/4, and the PCIOL in the right eye had trace posterior capsular opacification, while the left eye had 1+ nuclear sclerotic cataract. The dilated posterior segment evaluation of both eyes revealed a clear vitreous. The maculae were flat with a positive foveal

light reflex. The retinal vessels revealed mild attenuation in both eyes. Photos of the optic nerves can be seen in Figure 1.

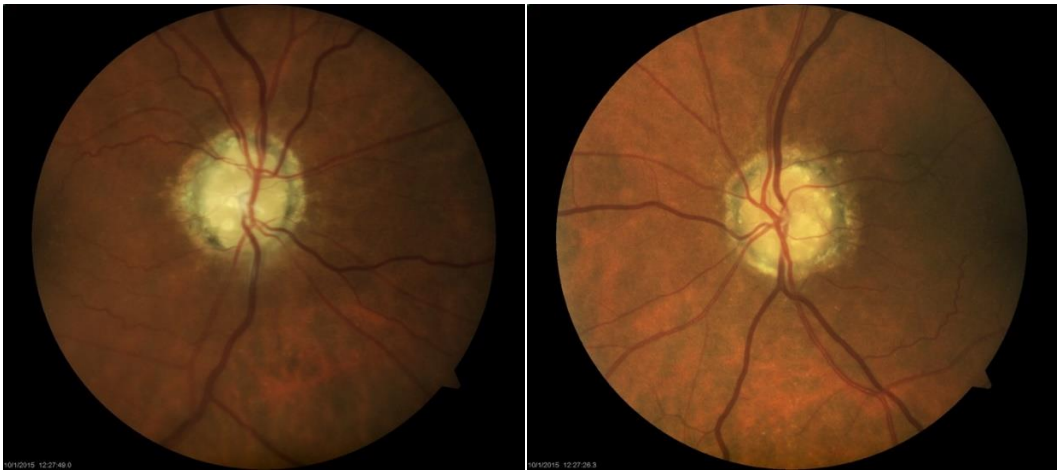

Figure 1. Optic nerve photos. OD (pseudophakic), OS (1+ NS cataract)

The differential diagnosis in this case includes:

1. Papilledema
2. Idiopathic intracranial hypertension (pseudotumor cerebri)
3. Toxoplasmosis
4. Anterior ischemic optic neuropathy
5. Optic nerve drusen (Optic disc drusen)

Papilledema is swelling of the optic nerve which is caused by elevated intracranial pressure. It frequently presents bilaterally, however, often asymmetrically.[1] The increased cerebrospinal fluid (thus increasing intracranial pressure) will result in axoplasmic flow stasis with intra-axonal edema seen at the optic disc.[2] Potential causes for papilledema include space occupying lesions, arterio-venous malformation, malignant hypertension, or infection.[1] If papilledema is present, it is necessary to begin the process of determining the etiology, as the etiology may be life threatening. In this case papilledema was ruled out because the vessels are clear at the optic disc margin.

Idiopathic intracranial hypertension (IIH) (occasionally pseudotumor cerebri)
To meet the definition of idiopathic intracranial hypertension, patients must meet these 5 criteria:[1]

1. Signs and symptoms of increased intracranial pressure

2. High cerebrospinal fluid pressure (>200 mm H_2O in non-obese patients >250 mm H_2O in obese patients) with normal CSF composition
3. Normal neuroimaging studies
4. Normal neurological examination findings (excluding papilledema or cranial nerve 4 palsy)
5. No identifiable cause (i.e., causative medication)

Patients who have true papilledema typically demonstrate at least one of the following clinical signs: enlarged blind spot, disc hyperemia, reduced physiological cup, a thickened nerve fiber layer obscuring blood vessels and peripapillary nerve fiber layer hemorrhages or retinal folds (Paton's lines).[1] Idiopathic intracranial hypertension presents with an elevated optic nerve head due to an increase in intracranial pressure. The diagnosis of IIH can be assumed at the time of presentation to an eyecare professional but, the necessary imaging, labs and procedures need to be performed to confirm the diagnosis. The pathophysiology of IIH is not well understood, but it occurs most frequently in obese women of childbearing age.[1,3,4] In this case, this diagnosis was ruled out due to a lack of symptoms and optic nerve appearance.

Toxoplasma gondii is a protozoan obligate intracellular parasite that is endemic to all land masses other than Antarctica.[5] Transmission to humans often occurs through exposure to cat feces from handling their litter, or through eating undercooked meat. The patient's exposure can be either acquired or congenital.[4,5] Signs vary based on whether the infection is active or dormant. Active signs include necrotizing retinitis, decreased vision, photophobia, floaters, vascular sheathing, full thickness retinal necrosis, "fluffy" white yellow lesion, overlying vitreous reaction, and anterior cells and flare. Presenting signs may also include disc edema, without choroidal lesions (resembling an optic neuritis appearance). Dormant toxoplasmosis appears as scattered atrophic chorioretinal scarsand gray-white "punched out lesions," which are often present at or near the macula.[4,5] Treatment is often not indicated unless the patient has active lesions in a location that may reduce vision. This was ruled out in our patient's case due to the lack of retinal abnormalities and optic nerve appearance.

Anterior Ischemic Optic Neuropathy (AION) is an ischemic infarction of the anterior portion of the optic nerve. Two prevailing theories regarding the pathogenesis of the infarction are proposed. The infarct may form secondary to occlusion of the posterior ciliary cilculation,[4,6] or because of a compartment syndrome which results in blood flow stasis through the optic nerve.[6] Nonarteritic implies that the infarction occurs in a patient absent of inflammation. A patient with this condition often awakens with unilateral, painless, vision impairment. The

patient may present with an afferent pupillary defect. Risk factors include hypertension, diabetes, hyperlipidemia, hyperhomocystinemia, and sleep apnea. Nocturnal hypotension is thought to have a role in patients who are taking anti-hypertensive medications.[4-6] The acuity upon initial presentation may vary over the following weeks with around 40% of patients improving over time and 10% of patients experiencing a further reduction in vision.[6] If the patient is presenting because of the acute onset of symptoms, care must be taken to rule out an arteritic cause and optic neuritis. Table 1[6] is useful in determining a patient's risk factors for arteritic and nonarteric optic neuropathy. Table 2[6] aids in determination of NAION with respect to optic neuritis.[6] The presence of optic disc drusen increase the likelihood of concomitant NAION.[6] Arteritic ischemic optic neuropathy was able to be ruled out because the patient denied pain, was without an APD, denies headache, scalp tenderness and jaw claudication. Non-arteritic anterior ischemic optic neuropathy was able to be ruled out based on the appearance of the patient's optic nerve and the lack of edema.

TABLE 1[6] ARTERITIC VS. NONARTERITIC OPTIC NEUROPATHY CHARACTERISTICS

Characteristic	**Arteritic**	**Nonarteritic**
Age	Mean 70	Mean 60
Sex	Female > Male	Female = Male
Associated Symptoms	Headache, scalp tenderness, jaw claudication, transient vision changes	None
Nerve appearance	Pallid edema, normal cup	Hyperemic edema, small cup
Erythrocyte sedimentation rate	Average 70 mm/hr	Average 20-40 mm/hr
C-reactive protein	Elevated	Normal
Fluorescein Angiography	Disc and choroid delay	Disc delay
Pain	(+) pain	(-) pain
Treatment	Systemic steroids	None

TABLE 2[6] OPTIC NEURITIS VS. NAION VS. ODD CHARACTERISTICS

Factor	**Optic Neuritis**	**NAION**	**ODD**
Age	<40	>50	Any age, more common in older patients

Pain	Likely upon rapid eye movement	None	None
Pupil	(+) APD	(+) APD	(-) APD
Visual field defect	Central	Altitudinal	Peripheral
Fluorescein Angiography	Normal disc	Delayed disc	If superficial will autoflouress, no leakage seen
MRI appearance	ON enhancement	Normal appearance	Difficult to image-better seen on CT

Optic Disc Drusen presents as a "lumpy-bumpy" appearance of the optic disc. There may be a hereditary link (autosomal dominant), and the buried hyaline-like material may calcify over time.[4,6,7] The drusen (if sufficiently superficial) appear hyperfluorescent with fundus autofluorescence. Its presence may result in visual field defects.

The appearance of the optic nerves (Fig 1) as well as the autofluorescence images below (Figure 2) were consistent with optic disc drusen. Upon close review of the vessels leaving the optic disc, no swelling is evident. This is consistent with stage 0 on the modified Friesen scale (Table 3).[8]

The patient did have hypertension and was currently on three separate medications for this condition. While toxoplasmosis can take a variety of forms there was a marked absence of retinal lesions or scars. Additionally, the patient denied any symptoms of inflammation over the time in question. Nonarteritic ischemic optic neuropathy would fit the symptoms displayed, however, on review of the images the presence of optic disc drusen was made apparent.

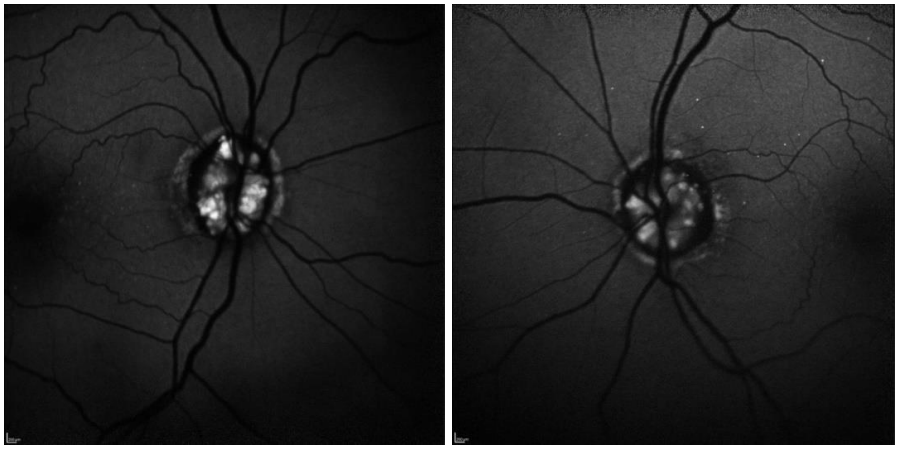

Figure 2. Fundus Autoflouresence Photos of Optic Nerves

Table 3[8] Modified Frisen Scale

Papilledema Grade	Findings
0	Normal Optic Disc
1	Minimal Papilledema: subtle C-shaped halo of disc edema with normal temporal margin
2	Low-degree papilledema: circumferential halo of disc edema
3	Moderate papilledema: obscuration of one or more segments of the major blood vessels leaving the disc
4	Marked papilledema: partial obscuration of a segment of major blood vessel on the disc
5	Severe papilledema: partial or total obscuration of all blood vessels on the disc

The patient was educated on the findings and prognosis associated with his diagnosis. With normal intraocular pressures, no treatment was recommended. He was scheduled to return in 2 weeks for an undilated Humphrey visual field 24-2 SITA standard OU to determine the presence of visual field loss. Additional diagnoses included a mild nuclear sclerotic cataract in the left yet, presence of pseudophakia in the right eye, and mild hypertensive retinopathy in both eyes.

FOLLOW UP #1

The patient returned for follow up on October 15, 2015, for an undilated exam with visual field. He denied any change in his health history. There were no changes to his ocular health. Copies of the automated visual fields are provided in Figure 3.

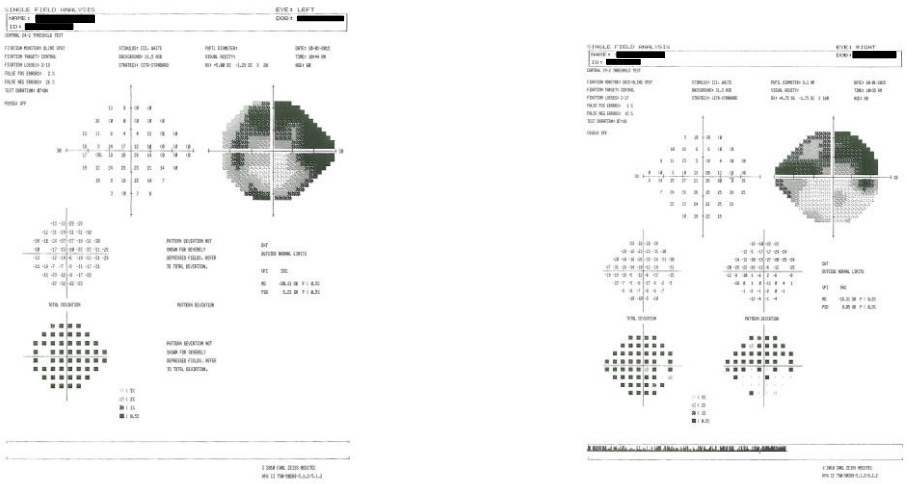

Figure 3. Humphrey visual field 24-2, OD & OS revealing visual field defects

The visual field results indicated a significant decrease in the patient's peripheral vision in both eyes. His visual acuities with correction (spectacles OD: +1.50-1.75x160 and OS: +1.75-1.25x020 / +2.50) were OD 20/50 and OS 20/20 with no improvement with pinhole. The combination of a decrease in the visual field and best corrected visual acuity resulted in the patient no longer meeting the requirements to maintain his commercial driver's license (CDL). He noted an increased difficulty in passing his vision test for the license over the prior three to four years. He was informed at this exam that his vision no longer met the minimum necessary vision required to maintain his license. The use of brimonidine 0.2% as an option to potentially slow the loss of vision (with neuroprotection as seen in the crushed rat model[9]) was discussed. The patient was presented with an informed consent detailing that the treatment was an off-label use of brimonidine, as brimonidine is FDA approved only for the lowering of intra-ocular pressures in patients with either ocular hypertension or open-angle glaucoma. The patient was amenable to the use of the drops and was initiated on a treatment regimen of brimonidine 0.2% in both eyes three times per day. The patient also indicated that he would need to speak to his human resources department regarding his vision. His next exam was set at one month to recheck intraocular pressures and aid with any necessary paperwork.

FOLLOW UP #2

The patient reported for a one month follow up on November 19, 2015. He had been using his drops with fair compliance (missing 3-4 drops per week) although he reported being more compliant the last few weeks. He noted that the drops irritated his eyes, and he did not feel like he was able to see any better (although he had been educated that they would not improve his vision). His distance vision with correction was stable at OD 20/50 and OS 20/20. There were no changes to his exam findings.

He brought along disability paperwork to be completed. The fact that the drops were not to improve vision but instead attempt to prevent further loss was again discussed. The patient declined to continue treatment at that time. Follow up visits were set at 4 months to reexamine visual fields and allow for further consideration of treatment. The patient has since been lost to follow up.

DISCUSSION

Optic nerve head drusen (or optic disc drusen, ODD) are acellular deposits of calcium, amino and nucleic acids and mucopolysaccharides that are located anterior to the lamina cribosa and are present in 0.3-2.4% of the population.[10] The drusen

are thought to develop as by-products of axonal metabolism in the affected population.[10] Drusen in this location may be present either superficially or "buried." Drusen located superficially are often easy to see upon examination (as in this case), however buried drusen are more difficult to determine, and may resemble papilledema, the latter representing a key differential diagnosis to rule out.

Disc drusen may appear in patients of any age and are often asymptomatic. In younger patients the drusen are often buried. As patients age the drusen become more superficial and more obvious during examination. The nature of this increasingly greater appearance has not yet been explained. Hypotheses include: drusen increasing in size, drusen migration to a more superficial location, or age-related thinning of the retinal nerve fiber layer.[10] The drusen's physical characteristics allow for a variety of imaging options.

No optic nerve OCTs were taken during the evaluation of this patient. In 2018, the Optic Disc Drusen Studies Consortium provided recommendations for an optic nerve OCT in patients with suspected optic nerve head drusen.[11] The recommendations include the following scan types: dense optic nerve head scan, radial optic nerve head scan, peripapillary scan, and macular scan. The consortium provided these recommendations to aid in establishing a reliable and consistent diagnosis of ODD for clinicians and researchers with the major concern being the differentiation between buried drusen and mild papilledema.

In a discussion of likely co-morbidities in patients with ODD, it is plausible that the patient may have had a previous NAION in the OD (as may be indicated by the difference in color on the optic disc photos). It is difficult to review the inter-ocular optic nerve photos relative to each other as the patient is pseudophakic in the right eye and had a 1+ NS cataract in the left eye. It is noteworthy that the presence of ODD in addition to the patient's vasculopathic history increases the likelihood of NAION. The patient being discussed did not present with an APD, would have been younger than the average age of a patient for NAION (based on the patient's history of when the vision decrease was first noted), and did not have a strictly altitudinal defect. It would have been difficult to determine whether a past NAION event had occurred as the patient met some of the criteria in Tables 1 and 2. A patient with ODD often has a crowded disc (due to the presence of drusen) as well as a narrowed Bruch's membrane which increases the likelihood of NAION. Due to this information, patients with ODD have a higher likelihood of a concomitant NAION which may present with combination of findings of both NAION and ODD.

IMAGING

Fundus Autofluorescence (FAF)

Fundus autofluoresence is a non-invasive technique to image the retina. The imaging is possible due to the presence of fluorophores. Fluorophores are naturally occurring molecules that absorb and emit light of specific wavelengths. Classical fundus autofluoresence uses blue-light excitation to elevate an electron to a high energy state. The emissions are then collected to form a brightness map representing the presence of fluorophore present in the imaged area.[10] If drusen are buried more deeply, more tissue is present between the drusen and the FAF imaging instrument. The deeper the drusen, the less obvious they appear.[12] Figure 2 demonstrates the image seen on FAF used to determine the presence of drusen in the patient in question.

B-scan

A B-scan uses high frequency sound waves to penetrate the eye. Similar to the use of blue light reflection in an FAF, sound waves are used to build a two-dimensional image of the eye. The sound waves are inaudible to humans because their frequency is higher than can be registered by the human ear. “Gain” is the ability to control the amplification of the incoming sound waves. As the gain is increased the depth of tissue penetrated increases as well. Adjusting the gain also helps the observer to determine densities of the objects in question.[13] This is demonstrated in the representative image presented in Figure 4.

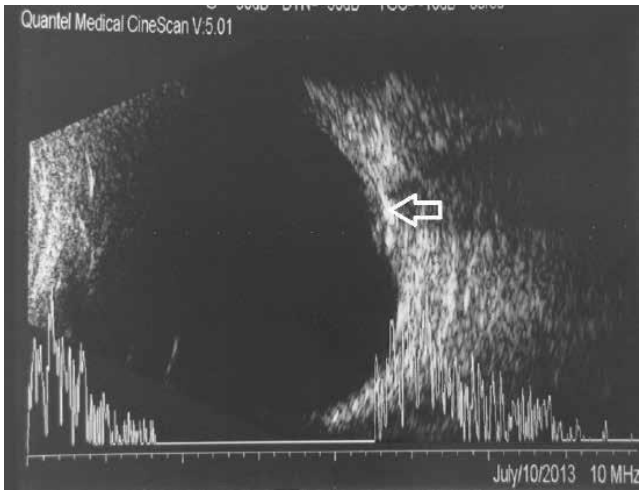

Figure 4.[11] B-scan of a patient with Optic Disc Drusen (seen as dense hyperfluorescent mass near the tip of the arrow, note the shadow to the right indicating the structure of the optic nerve)

Computed tomography (CT) of the orbit

Imaging via CT is another test which can reveal the presence of optic disc drusen.[12] The calcium present within the drusen hyperfluoresses under x-rays used to assemble the image of a CT as seen in Figure 5. However, while a normal CT is performed in 1.5 mm sections, finer striations should be ordered to reduce the likelihood of missing the drusen.[8] It is the experience of the author that optic disc drusen are usually seen on CT only as a secondary finding rather than being the purpose of the test.

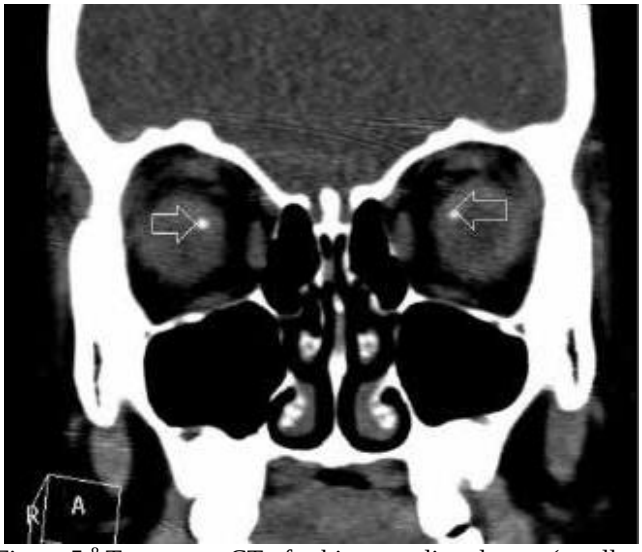

Figure 5.[8] Transverse CT of orbits revealing drusen (small dense white masses as indicated by arrows)

The accuracy, flexibility, and low cost of using a B-scan in order to determine the presence of either superficial or buried drusen suggests that this should be the preferred imaging method to confirm the findings for many providers.[14]

MONITOR

Vision loss may occur (or worsen) as a patient with ODD ages. It has been established that as a patient ages, the thickness of the retinal nerve fiber layer decreases due to normal axonal cell death.[15] The appearance and effect that optic disc drusen has on a patient's vision is secondary to a few characteristics. Initially, the appearance of ODD is less noticeable fundoscopically in younger patients. As the patient ages more drusen appear superficially. A study presenting 50 children with ODD showed superficial drusen were present in only 18% of children between the ages 7-10 years old, however, that number increased to 37% in patients aged

11-14.[15] The change in the appearance of superficial drusen does not seem to continue to increase much beyond this age. As the patient ages, visual fields become more important in monitoring the patient. A limited study (8 patients) showed a decrease in retinal sensitivity of 27%.[16] Retinal sensitivity is, however, also known to decrease over time even in patients without ODD. In patients over the same time frame studied, retinal sensitivity is shown to decrease 11.9%.[16] Presumably the remaining decrease of 15.1% could be due to progressive vision loss secondary to optic disc drusen.[16]This study's most obvious limitation is the low number of patients followed, although the authors did maintain follow up visits with the patients over a remarkable 56-year span. Further evaluation of a larger population would be helpful to confirm these findings.

Neuroprotection

Neuroprotection denotes the use of therapeutics to improve the neuronal survival and preservation of function.[16] Medicine has had many failed treatments regarding this promising idea. Additionally, the difficulty of replicating results found in animal studies has been disappointing.[16] The most common ocular example is of brimonidine, an alpha 2 adrenergic agonist that is commonly used to decrease intraocular pressure. Brimonidine was shown to be protective of retinal ganglion cells in crushed rat nerves. However, the results of the Low-pressure Glaucoma Treatment study did not reaffirm these benefits.[17] We have seen similar failures in the arena of neuroprotection with drugs like memantine, ciliary neurotrophic factor, and most recently lampaizumab.[18] While each drug showed promise in various preliminary studies, further research failed to confirm these results. Unfortunately, this seems to have led to skepticism about future neuroprotection options. It seems wise to continue to use the aforementioned set back as learning opportunities rather than the hard stops they may seem. There are currently different drugs in both phase I (recombinant human nerve growth factor) and II (CNTF) clinical trials examining neuroprotection in glaucoma.[18]

CONCLUSION

This case demonstrates the role of a careful optic nerve evaluation, timely imaging, and differential diagnosis for potential causes of optic nerve edema. In many cases of ODD, careful examination and use of the most recent testing guidance can result in a correct determination of the cause of pseudopapilledema. Judicious use of testing and diagnostic imaging is important in maintaining high quality care with minimal cost. While there is not a currently effective treatment for patients with ODD, correct diagnosis and social assistance may help patients to maintain a lifestyle with which they are comfortable. While the shortcoming of

neuroprotection has been noted, it may be appropriate for the provider to present the patient with some treatment option as long as an accurate cost benefit analysis has been provided. As patients with ODD may continue to exhibit decrease in vision throughout their adult lives, annual examination with visual field analysis is indicated.

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