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Bilateral Optic Disc Drusen with Neuroretinitis

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Bilateral Optic Disc Drusen with Neuroretinitis

Abstract

Background: Neuroretinitis is an inflammation of the posterior pole of the eye, resulting in optic disc edema and macular star formation. Systemic conditions associated with these findings include tuberculosis, toxoplasmosis, syphilis, lyme disease, toxocariasis, mumps, herpes simplex, and cat scratch disease. This case illustrates diagnosis and treatment for a patient with neuroretinitis complicated by preexisting vision loss.

Case Report: A Caucasian male in his 40's presented to the eye clinic for an emergency appointment with complaints of constant blurry vision, especially inferiorly upon awakening, in his right eye for the past two weeks. His ocular history included optic disc drusen in both eyes with profound peripheral vision loss in the left eye. The patient's systemic history included cluster headaches and sleep apnea. Entering visual acuities were 20/150- OD and 20/20 OS. Additional medical history questioning revealed the recent adoption of a kitten.

Conclusion: This case describes the diagnosis and treatment for the rare condition of neuroretinitis secondary to a Toxocara infection. While cat scratch disease was initially suspected, detailed laboratory testing identified the true, and more rare, causative infectious agent. A variety of differential diagnoses were ruled out through laboratory and imaging studies. Consultations with neuro-ophthalmology and infectious disease specialists were exceedingly valuable in contributing to a positive outcome for this patient. This patient's preexisting ODD with vision loss heightened the concern to preserve the patient's remaining vision and further added to the complexity of this challenging case. The importance of medical history questions regarding animal contact also proved vital for accurate diagnosis and treatment of this sight threatening condition.

Keywords

Neuroretinitis, macular star, drusen

INTRODUCTION

Neuroretinitis is an inflammation of the posterior pole of the eye, resulting in a classic triad of acute painless unilateral vision loss, optic nerve edema, and macular star formation.[1] The inflammation begins as a vasculitic process in the optic nerve due to infectious or immune-mediated etiologies. Numerous systemic conditions can be associated with these findings including tuberculosis, toxoplasmosis, syphilis, Lyme disease, toxocariasis, mumps, herpes simplex, and cat scratch disease. Additionally, diagnosing neuroretinitis can be clouded by other mimicking ophthalmic conditions. This case illustrates treatment for a patient with neuroretinitis complicated by preexisting vision loss. Appropriate laboratory tests and differential diagnoses will also be described.

CASE REPORT

A Caucasian male in his 40's presented to the eye clinic for an emergency appointment with complaints of constant blurry vision in his right eye upon awakening for the past two weeks. In the same eye, he also noted grey vision inferiorly and light sensitivity. Eight years prior, the patient was diagnosed with pseudo-papilledema secondary to buried optic disc drusen (ODD) following computed tomography (CT), lumbar puncture, and intravenous fluorescein angiography (IVFA) to rule out space occupying lesions and true optic disc edema. At the time of diagnosis, crowded, elevated optic nerves were noted in each eye, with peripheral vision loss in the left eye. Prior fundus photos (figure 1), Humphrey visual field (HVF) tests (figure 2), and retina nerve fiber analysis (RNFL) reports (figure 3) were available in his medical record.

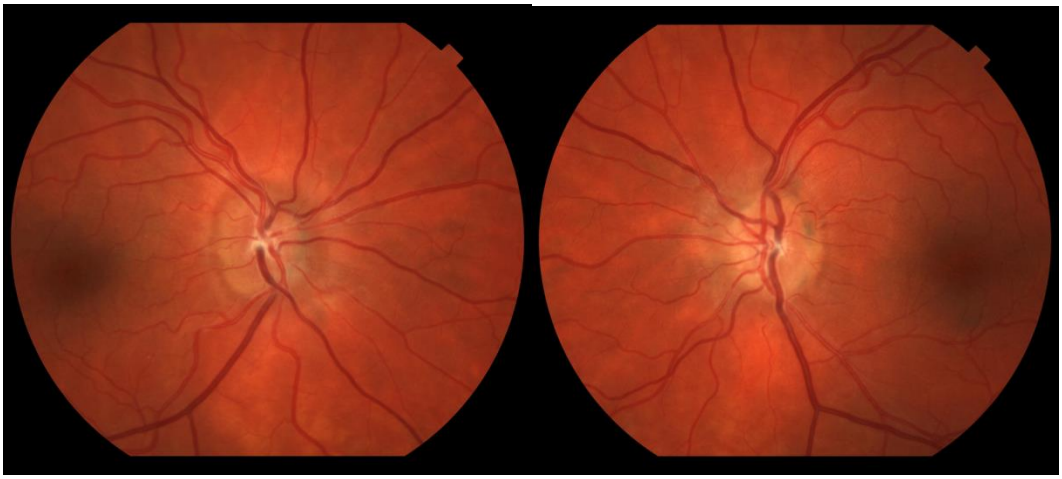

Figure 1: (Baseline: two years prior) The color images of the right and left eyes reveal full, elevated, optic discs as evidenced by the blood vessels cascading over the distinct disc margins onto the peripapillary retina.

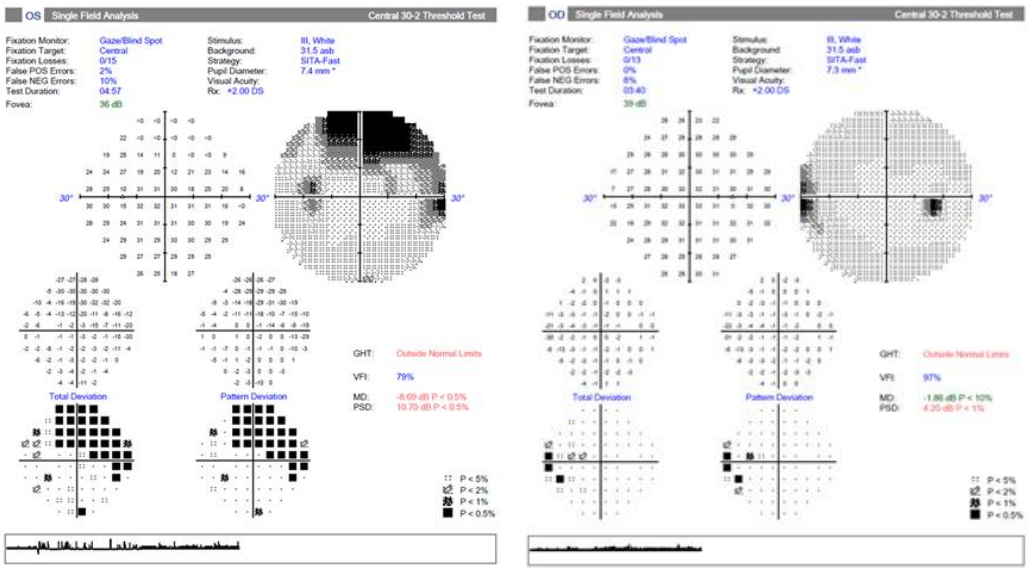

Figure 2: HVF 30-2 (Baseline: two years prior) The visual field of the right eye shows a nasal defect greater inferiorly with a solitary inferior nasal point defect. The visual field of the left eye shows a dense superior arcuate defect containing numerous absolute losses associated with an early inferior nasal step. The reliability is borderline due to false negative errors.

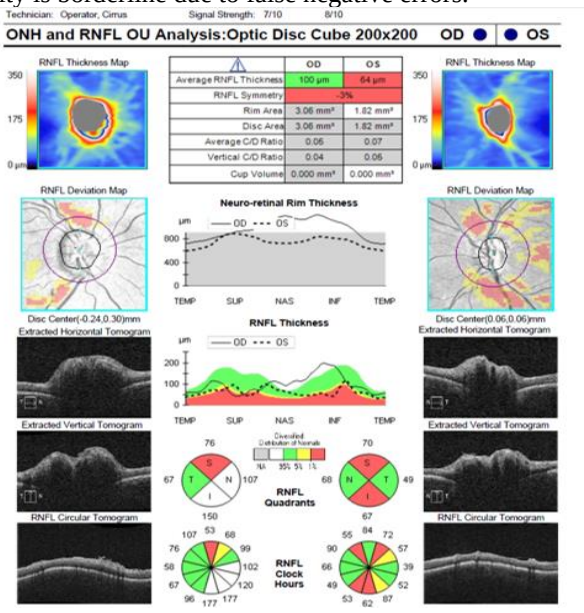

Figure 3: RNFL (two years prior) The report demonstrates asymmetry in the measured optic disc size and peripapillary RNFL thickness between the right and left eyes. Note the superior quadrant thickness averages are similar between the eyes, however, there is advanced thinning of the left eye inferiorly which accounts for the superior visual field defect demonstrated on the threshold visual field test of the left eye. The horizontal and vertical tomograms demonstrate the elevated, full optic nerves.

The patient's systemic history included cluster headaches and sleep apnea, with a notation of nonadherence for sleep apnea treatment. The patient's social history revealed cigarette smoking 1.5 packs per day for 25 years, social alcohol consumption, and no illicit drug use. Additionally, he reported adopting a new kitten approximately 11 weeks prior. He denied any animal bite or scratch history but did recall handling several animals in the shelter during the adoption process.

Entering uncorrected visual acuities were 20/150- OD and 20/20 OS. There was no improvement with pinhole OD. Ocular motility was smooth and full, without diplopia or pain. Pupils were equal and reactive, with a mild RAPD OD. The external examination revealed normal slit lamp findings with quiet anterior chambers and clear lenses OU. Internal examination of the right eye revealed 2+ vitreous cells, elevated optic nerve head margins, and macular edema with exudative star formation in the right eye (see figure 4). The peripheral retina was intact OU. In-office blood pressure measured 122/81mm Hg.

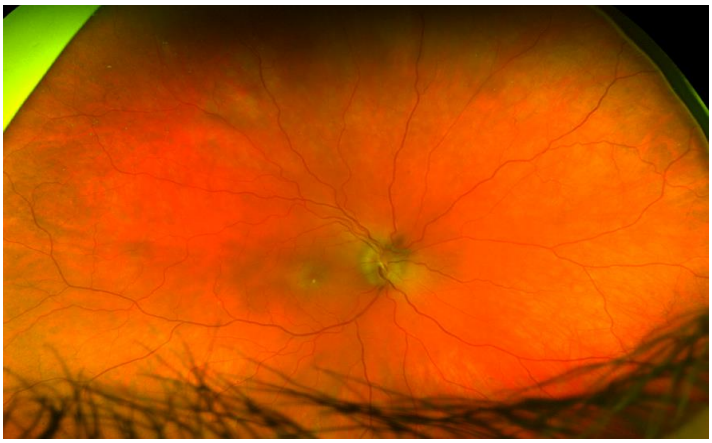

Figure 4: Right eye with neuroretinitis The color image demonstrates blurring of the disc margins and presence of exudation in the fovea forming an early macular star surrounding a larger, central foveal exudate. Additionally, there is a vitreous floater and small, discrete, pinpoint sized retina pigment epithelial defects visible within the posterior pole inferior and temporal to the macula.

The internal examination of the left eye revealed a full and distinct nerve with flat macula, normal vasculature and intact retina periphery (see figure 5).

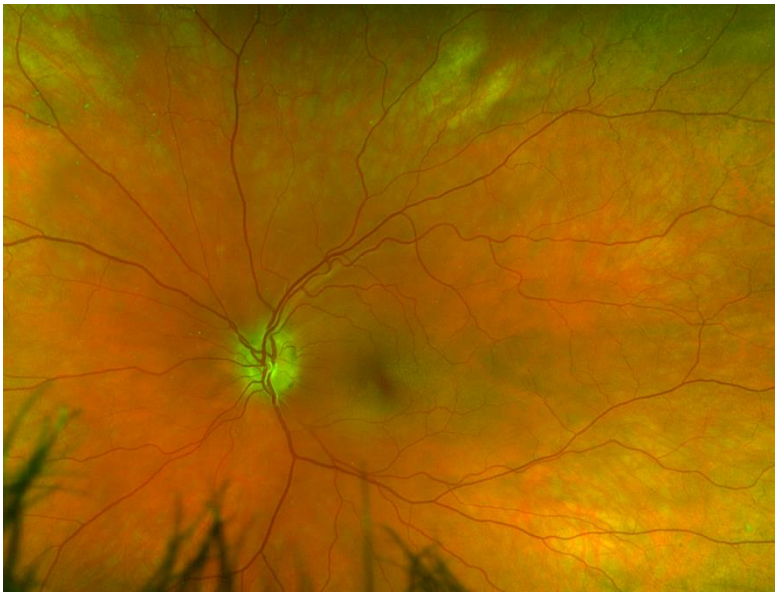

Figure 5: Left eye stable from baseline-The color image shows the stable nerve and fundus appearance of the left eye when compared to the baseline posterior pole image. Note in this image a subtle window defect superior to the optic disc seen under a retina arteriole. Additionally, there are small, discrete pinpoint areas of RPE dropout throughout the fundus.

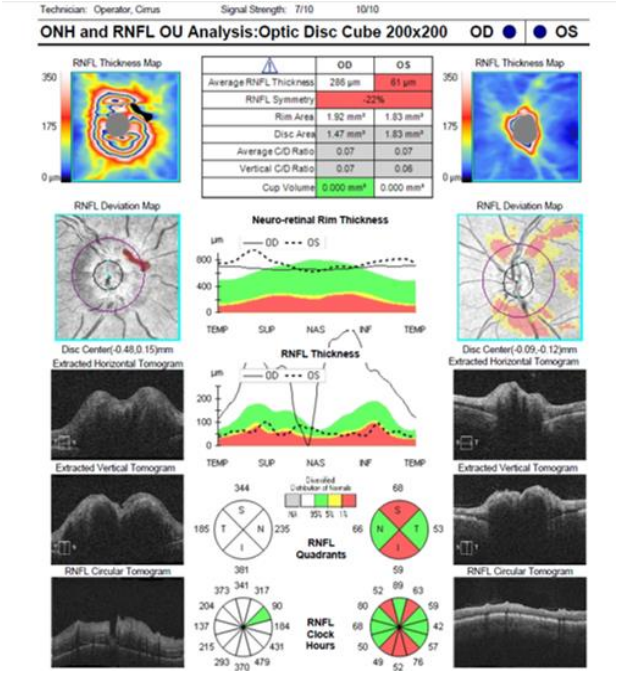

Figure 6: RNFL (day of emergent visit) This report demonstrates a relative increase in the peripapillary RNFL thickness of the right eye. Note the ringlike pattern surrounding the optic disc

(Figure 6 cont.) on the thickness map. The left eye's thickness map is similar to baseline with the exception of the inferior quadrant which appears to show progressive thinning.

The RNFL analysis revealed an increase in peripapillary RNFL thickness compared to baseline in the right eye (see figure 6). The left eye retinal nerve fiber layer thickness remained stable to baseline.

The macular thickness analysis report showed intraretinal and subretinal macular edema with a foveal center thickness of 376 microns OD (see figure 7).

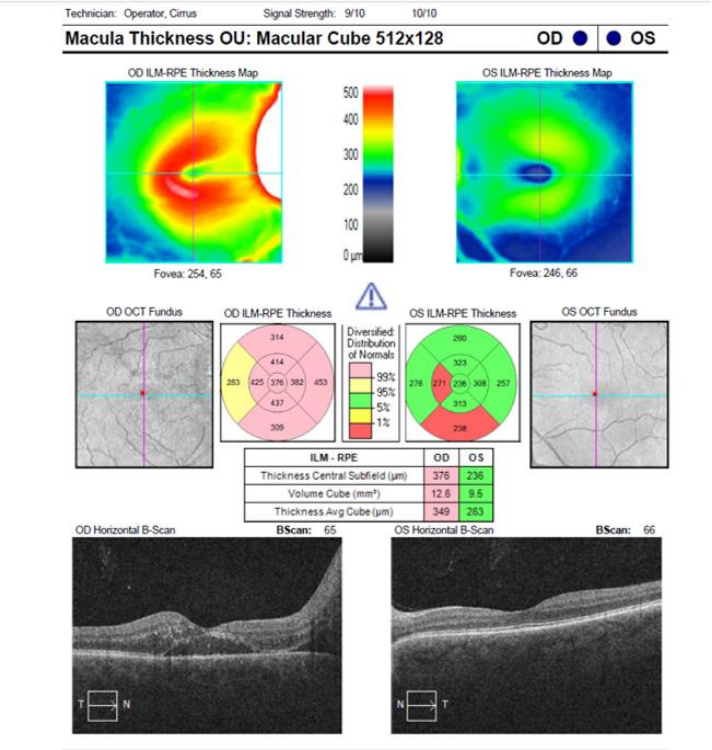

Figure 7: Macular thickness analysis report emergent visit - The macula thickness scan demonstrates subfoveal and subretinal fluid near the temporal margin of the optic nerve of the right eye. Additionally, hyperreflective, intraretinal deposits can be identified in this scan along with the presence of a vitreous cell. The left eye horizontal b scan shows a relatively normal cross section of the macula within this line scan of the left eye.

A HVF 30-2 test of the right eye revealed an enlarged blind spot corresponding to the optic disc edema and peripapillary subretinal fluid, and a paracentral visual field defect correlating to the presence of macular edema which is greater in the inferior macula. The severe superior and inferior nasal visual field defects are presumably from induced ischemia occurring at the optic disc due to reduced axoplasmic flow and swelling of the ganglion cell axons,[2] made worse by the crowding and presence

of ODD in this eye. The threshold visual field of the left eye is reliable and shows a severe, superior arcuate defect with early nasal step. Compared to baseline, this visual field appears to be worse in the size and the depth of the defect as evidenced by the number of absolute losses. This correlates to the RNFL report showing progressive thinning of the inferior quadrant's RNFL thickness. (see figure 8).

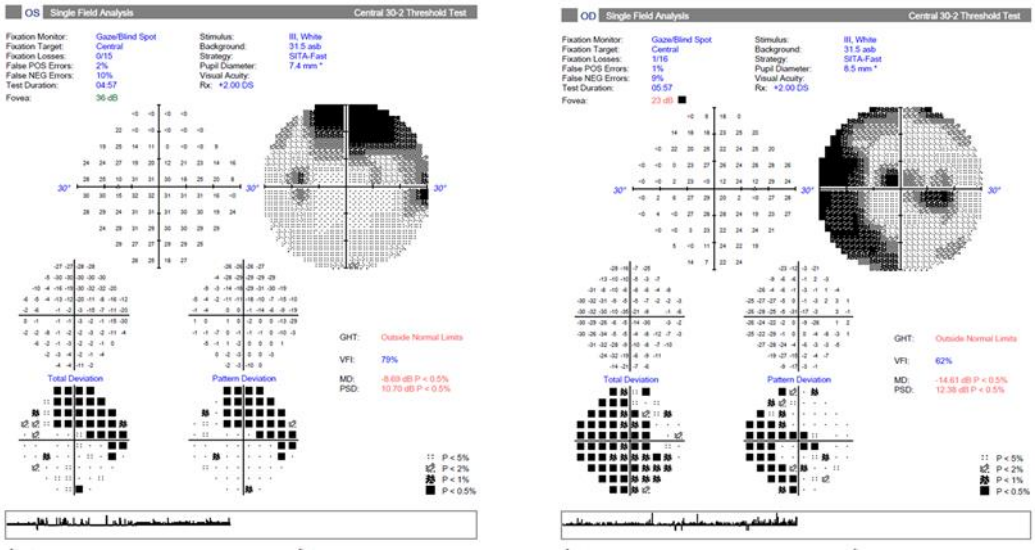

Figure 8: HVF 30-2 emergent visit

Intravenous fluorescein angiography (IVFA) was ordered that day and revealed early leakage and late disc staining of the right eye without macular leakage. The left eye revealed normal results highlighting a small retina pigment epithelium (RPE) window defect in the superior retina.

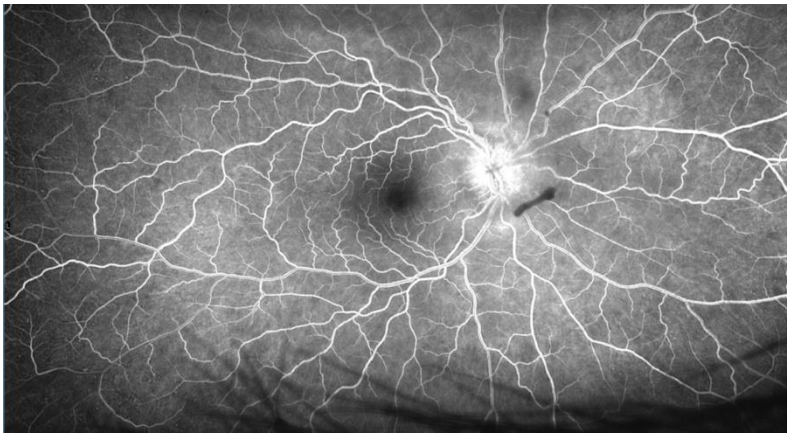

Figure 9: IVFA right eye midphase – The fluorescein angiography image demonstrates

(Figure 9 cont.) hyperfluorescence of the disc and disc vasculature. The arteriolar phase is complete and the venous phase is mid to late with evidence of some residual laminar flow. The macula does not show leakage and there are pinpoint areas of hyperfluorescence scattered in the periphery consistent with the presence of minute RPE defects observed in earlier color fundus images. The irregular shaped dark area inferior nasal to the disc is an artifact from the vitreous.

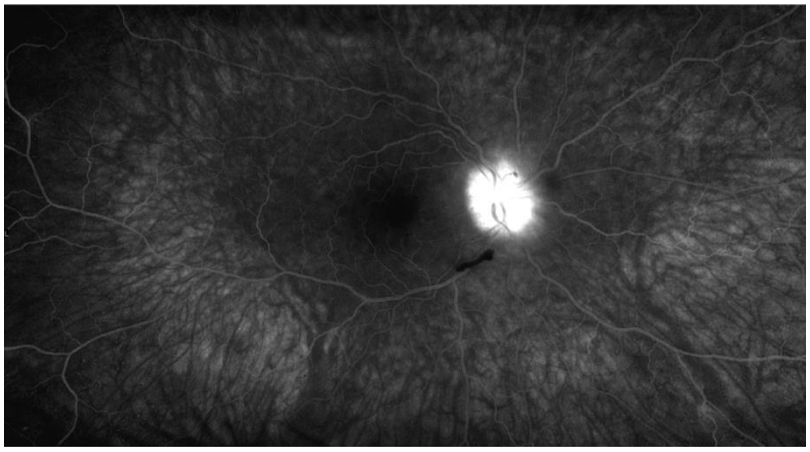

Figure 10: IVFA late phase right eye – The optic disc continues to glow in the late phase of the study confirming the presence of disc edema. The macular region remains hypofluorescent without late macular leakage.

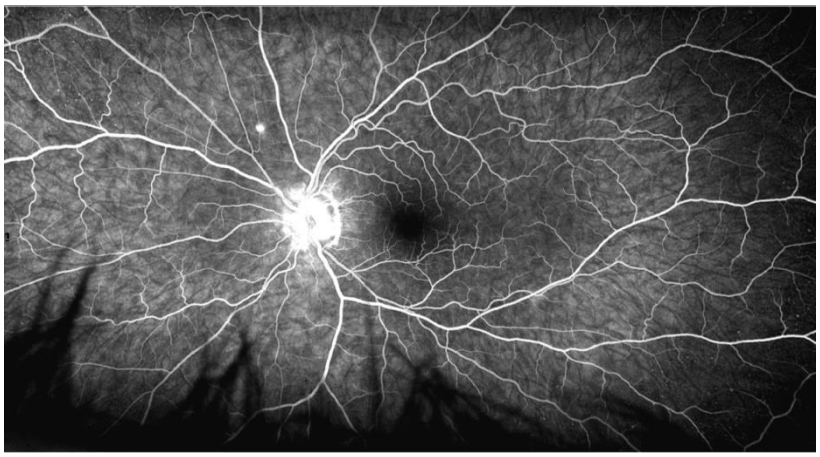

Figure 11 IVFA left eye – The mid phase angiography image for the left eye demonstrates a hyperfluorescent disc with hyperfluorescence in the areas of peripapillary atrophy as well as the window defect noted superiorly to the nerve. The macular region is Hypofluorescent without leakage. Several pinpoint sized RPE defects are observed in the retina periphery.

Laboratory orders included a complete blood count (CBC) with differential, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), tuberculosis (TB) testing, toxoplamosis antibody testing, rapid plasma reagin (RPR), toxocara

antibodies, Bartonella antibodies, angiotensin converting enzyme (ACE), and lysozyme. A neuro-ophthalmology appointment was scheduled for the following day.

NEURO-OPHTHALMOLOGY VISIT 1

The patient returned the next day with unchanged visual acuity, history, and ocular status OU. Lab results from the prior day revealed a slightly elevated CRP, normal ESR, negative syphilis screening, and essentially normal CBC with differential. Lymph nodes were checked in the office and were found to be normal. However, the patient reported a "knot" in his right jaw roughly two weeks prior that resolved in about one day. The patient was tentatively diagnosed with cat scratch disease (CSD) and after discussing risks and benefits was started on oral doxycycline 100mg bid and rifampin 300mg bid for two weeks.

Additional laboratory orders were placed for liver function tests (due to the rifampin order), herpes simplex virus (HSV) IgM antibodies, varicella zoster (VZV) IgM antibodies, and the patient was scheduled for a progress check in two weeks. Lab results returned with normal and negative findings for all tests with the exception of toxocara antibodies. The neuro-ophthalmologist was alerted about the test results and requested a consultation for the patient with an infectious disease (ID) specialist. The patient was also contacted with the lab results and notified of the recommended infectious disease consult. Two days later the patient phoned the clinic to report he had his cat tested for toxocara and the results were negative.

NEURO-OPHTHALMOLOGY VISIT 2

Two weeks later the patient returned with stable vision, history, and ocular status. Plans included stopping oral doxycycline and rifampin and to keep his scheduled infectious disease consult for later that same day. The patient was diagnosed with neuroretinitis due to toxocariasis.

INFECTIOUS DISEASE CONSULTATION SUMMARY

The patient was examined, and the following tests were ordered: MRI brain, CT chest/abdomen to rule out visceral larva migrans (VLM), and lumbar puncture (LP). Additional blood work included strongyloides antibodies, Epstein-Barr Virus (EBV), cytomegalovirus (CMV), and human immunodeficiency virus (HIV). Lab testing, MRI brain, and CT abdomen results were all negative. The ID specialist initiated treatment for toxocariasis. The patient was placed on oral albendazole 800 mg daily for thirty days and oral prednisone tapered as follows: 60 mg daily for 7 days, then 40 mg daily for 7 days, then 20 mg daily for 7 days, then 10 mg daily

for 7 days, then 5 mg daily for 7 days, and then discontinue. The patient was re-examined 5 weeks later by the ID specialist and released back to neuro-ophthalmology.

NEURO-OPHTHALMOLOGY VISIT 3

Three months after the initial visit the patient returned with stable vision (20/150 OD and 20/20 OS) and medical history. The RNFL and macula scan reports showed a reduction in optic nerve swelling and macular edema of the right eye. No further treatment was indicated, and the patient was advised to return in one month for follow up.

NEURO-OPHTHALMOLOGY VISIT 4

The following month the patient returned with greatly improved uncorrected vision in the right eye to 20/25 and stable vision in the left eye at 20/20. The macula thickness remained stable OD, OS. The patient was advised to return in 3 months for a follow-up visit.

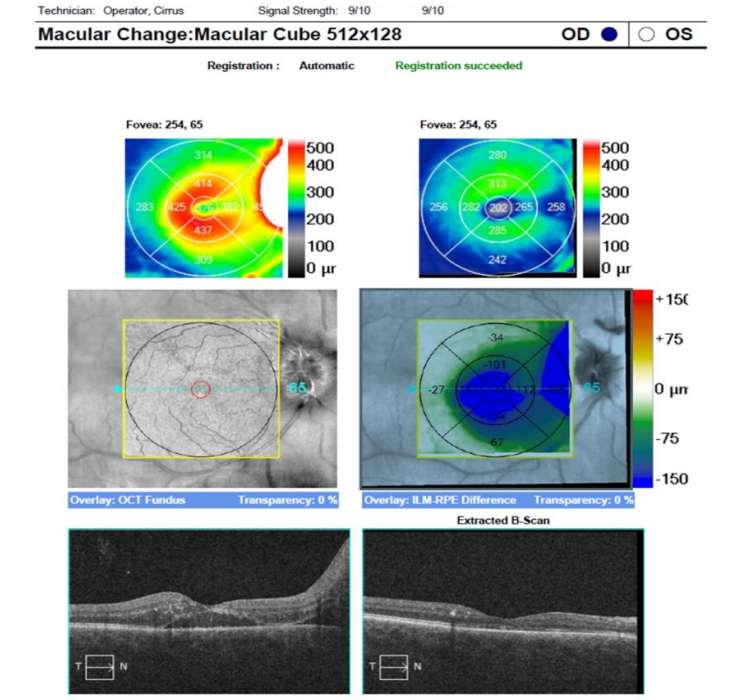

Figure 12: Macula change analysis report right eye - The macula change analysis report shows a drastic reduction of retinal edema from the initial emergent visit to four months (Figure 12 cont.) later, restoring normal retinal architecture and function as evidenced by improved visual acuity. A residual, intraretinal, hyperreflective deposit is observed in the cross section of this image representing a hard exudate.

NEURO-OPHTHALMOLOGY VISIT 5

Seven months after the initial visit the patient returned with complaints of blurry distance vision in the right eye and altered depth perception. Unaided acuity was 20/20- OD and 20/20 OS. Amsler grid testing revealed subtle metamorphopsia in the right eye and normal findings in the left eye. The macula thickness scan was stable with the presence of fine scattered hyperreflective deposits in the right eye. The left eye remained unchanged. Plans included monitoring the patient's status in 6 months with the neuro-ophthalmologist with no further treatment indicated.

DISCUSSION

Distinguishing optic disc drusen from early disc edema can be a challenging task. It is worth reviewing ODD in light of our patient's history and initial clinical presentation, particularly due to the pre-existing vision loss in the left eye, and the onset of new vision loss in the right eye.

Drusen of the optic disc have been described for over 100 years in the ophthalmic literature.[3,4] **"**Druse" is a word of German origin describing a crystal lined hollow space in a rock.[5] Clinically, disc drusen near the surface are easily diagnosed by their characteristic lumpy appearance. They are often located more nasally[4] in the optic nerve and can be confirmed with additional tests including fundus autofluorescence imaging (FAF), ultrasonography, and OCT. The incidence of clinically diagnosed disc drusen has been estimated to be 0.3-0.5%.[6] Disc drusen below the surface may go unnoticed clinically. Surface drusen tend to be more common in older patients and these nerves proportionally are prone to have a greater volume of ODD compared with those whose drusen are "buried."[7] Optic disc drusen may resemble optic disc edema and on occasion may present with disc hemorrhage and visual field defects.[8]

If optic disc edema is suspected in a patient with pre-existing ODD, one way to determine if there is a status change is to review baseline RNFL scans for comparison (as in our patient). Furthermore, changes in the RNFL values can be analyzed to aid diagnosis of worsening disc edema in the presence of disc drusen and utilized again over time to assess RNFL loss from axonal damage following an episode of disc edema.[7]

Optic disc drusen appear on OCT as internally hyporeflective structures with a full or partial hyperreflective margin superiorly. They are located anterior to the lamina cribrosa and they may occur in clusters or single entities and are often adjacent to the nasal border of optic disc.[9,10]

The analysis and composition of ODD has consistently shown the presence of calcium.[4,6] There are reports in the literature of hereditary tendencies [4,5] with bilateral presentations occurring up to 80% of the time.[4] Optic disc drusen can compress axons of the optic nerve.[3] ODD may cause a crowding effect leading to physical changes in the nerve promoting RNFL loss and subsequent VF defects.[11,12] VF defects have been shown to be more prominent with superficial ODD and present in up to 87% of patients diagnosed with ODD.[5] Additional ODD complications may include anterior ischemic optic neuropathy(AION), choroidal neovascular membranes (CNVM), hemorrhages, and central retinal artery or vein occlusions.[5,6] Optic disc drusen may be an independent risk factor for non-arteritic anterior ischemic optic neuropathy (NAAION).[12] There are multiple disease associations both ocular and systemic with ODD, including retinitis pigmentosa (RP), pseudoxanthoma elasticum (PXE), and angioid streaks. [5,6]

Challenges may exist in the OCT interpretation of ODD since they may be confused with peripapillary hyperreflective ovoid mass-like structures (PHOMS) or blood vessel lumens.[7,10] Although oval and hyperreflective, PHOMS do not show a hollowed central core like ODD, do not autofluoresce, and cannot be distinguished with ultrasonography. They are presumably composed of herniated axons within the peripapillary region of the optic nerve.[13] Blood vessel lumens can be recognized by a more densely hyperreflective surface from their vascular walls. Their columnar shadowing and the ability to cross reference their location on the optic disc will help to differentiate them from ODD.

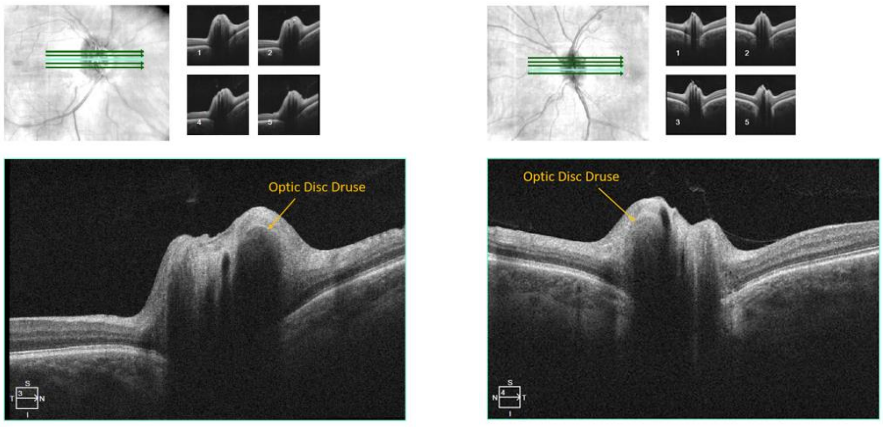

Figure 13: Baseline OCT line scans right eye and left eye - The patient's baseline high definition line scans of the right and left eye two years prior. Note the hyperreflective surface signal followed by the hyporeflective core on the images.

Neuroretinitis was first described in 1916 by Leber who termed the condition idiopathic stellate maculopathy after believing it to be a disorder of the macula.[1,14] It was later determined by Gass that the optic nerve was affected prior to the presentation of the macular star, suggesting “neuroretinitis" as a more appropriate descriptor.[1] The classic clinical triad of neuroretinitis is characterized by acute unilateral vision loss, optic nerve edema, and the formation of a macular star due to the arrangement pattern of macular exudates.[1,15] This inflammation of the optic nerve and peripapillary retina may also present with a vitritis and other deep white retinal lesions.[1,16]

Neuroretinitis begins as a vasculitic process in the optic nerve that causes leakage of lipid-rich fluid through the outer plexiform layer of the retina which leads to the formation of the macular star.[15,16] While macular exudates may not be clinically evident until up to six weeks following the onset of symptoms, earlier detection using optical coherence tomography and fundus autofluorescence can aid in a more timely diagnosis.[1] Neuroretinitis affects all ages, but more often in the third and fourth decades of life.[15] Visual acuity at presentation ranges from 20/20 to light perception.[15] The most common visual field defect is a cecocentral scotoma, but central scotomas, arcuate defects and even altitudinal defects may also be present. An afferent pupil defect RAPD is present in most patients unless bilateral.[15]

The etiology of neuroretinitis is thought to be infectious or immune mediated.[15] While neuroretinitis often presents with a viral prodrome, viral agents are rarely discovered from these cases.[15] Herpes simplex, hepatitis B, mumps, herpetic acute retinal necrosis syndrome, and cytomegalovirus have been listed as potential viral causes.[15,17]

Neuroretinitis is often misdiagnosed.[15] One study found that as many as 35% of neuroretinitis case referrals were actually other diseases presenting with optic nerve edema and a macular star.[1] The most common mimicker was malignant hypertension (43%), followed by idiopathic intracranial hypertension (14%), diabetic papillopathy (14%), branch retinal vein occlusion (12%), and finally anterior ischemic optic neuropathy (7%).[1] Diagnosis can be further complicated due to the lack of macular star formation at initial examination. Stellate macular exudates typically occur 2-6 weeks following onset of the optic nerve edema. [1]

Neuroretinitis presents unilaterally, in contrast to many of the differential diagnoses which present bilaterally. Malignant hypertension is typically bilateral, but may be asymmetric.[18, 19] Idiopathic intracranial hypertension (IIH) can also result in papilledema with secondary macular edema due to both mechanical and hemodynamic changes at the optic nerve spreading to the peripapillary area and macular region.[20] In the presence of bilateral disc edema, a space occupying lesion

must be ruled out. If imaging rules this out, infiltrative etiologies should also be considered. However, it is more common for infiltrative neuropathies to present unilaterally, with a more nodular or mass-like appearance of the optic nerve and with more severe vision loss.[21,22] Papillitis associated with multiple sclerosis presents with optic nerve edema in about one third of optic neuritis cases. These cases rarely have an associated macular star, especially prior to a definitive diagnosis of multiple sclerosis.[23]

Anterior ischemic optic neuropathy may also be mistaken for a neuroretinitis as it involves unilateral painless vision loss with associated optic nerve edema.[15] Macular edema is rare in this condition, but spillover edema from the optic nerve is possible.[24] Nonarteritic ischemic optic neuropathy, arteritic anterior ischemic optic neuropathy (AAION), giant cell arteritis, and central retinal vein occlusion should all be considered in the differential diagnosis of neuroretinitis.

	Neuroretinitis	**Malignant Hypertension**	**Idiopathic Intracranial Hypertension**	**Diabetic Papillopathy**	**Retinal Vein Occlusion**	**Anterior Ischemic Optic Neuropathy**	**Papillitis**
Laterality	Unilateral	Bilateral	Bilateral	Unilateral or Bilateral	Unilateral	Unilateral	Unilateral
Pupils	(+)APD	(-)APD	(-)APD	(-)APD	(+)APD, depending on severity	(+)APD	(+)APD
Physical examination	Disc edema, macular star, possible vitritis	Disc edema, macular star	Disc edema, possible macular star	Disc edema, often with severe diabetic retinopathy	Hemorrhaging, exudates, possible macular and disc edema	Disc edema, rarely macular edema	Disc edema
Symptoms	Fever, fatigue, headaches, lymph node swelling	Headache, nausea, chest or back pain, dyspnea, orthopnea	Headaches, nausea, dizziness, neck pain	Often asymptomatic	Often asymptomatic	Arteritic: scalp tenderness, jaw claudication, temporal pain	Pain with eye movement, balance problems, fatigue, bladder dysfunction
Risk factors/ Associations	Exposure to infectious or parasitic diseases, animal or insect bites, raw meat ingestion	Uncontrolled blood pressure, >180/120	Female, obesity, endocrine disorders	Uncontrolled type 1 or type 2 diabetes	Hypertension, hyperlipidemia, diabetes, increasing age, blood hyperviscosity, open angle glaucoma	Giant cell arteritis, crowded nerves, sleep apnea, nocturnal hypotension, smoking	Multiple sclerosis

Table 1: Common differentials and misdiagnoses of neuroretinitis [1,15,30,31,32]

Our patient was initially diagnosed with and treated for cat scratch disease based on the presence of neuroretinitis and the patient's history of a recent kitten adoption. Cat scratch disease is the most common infectious cause of neuroretinitis and is caused by Bartonella henselae, a gram-negative bacillus, contracted through cat bites or scratches.[1,16,28] In 2016 it was estimated that 12,500 individuals are

diagnosed with CSD annually in the United States.[29] Most patients diagnosed with CSD report a history of close contact with cats.[17] It is often self-limiting and presents with a papule at the inoculation site several days after the break in skin. Regional lymphadenopathy follows in 90% of cases, and systemic symptoms such as fever, fatigue, and headaches occur in about 50% of cases.[29,28] Atypical manifestations, occurring in about 10% of CSD patients, include neurologic, dermatological, musculoskeletal, hepato-splenic, and most commonly, ophthalmic involvement.[29,28]

Several inflammatory ocular conditions are associated with CSD. A large study found 88% of ocular CSD presented with swollen optic nerves; 79% of these cases were diagnosed with neuroretinitis at some point in the disease presentation, making neuroretinitis the most common ophthalmic manifestation of CSD.[29] Other ophthalmic findings included: parinaud oculoglandular syndrome, anterior uveitis, retrobulbar neuritis, chorioretinitis, retinal vessel occlusion, and panuveitis.[29] One study found that the presence of a peripapillary serous retinal detachment in the presence of optic disc edema may be an early sign of *B. henselae* infection even in the absence of associated chorioretinitis and macular star formation (which may take weeks to develop).[30]

Treatment of ocular CSD has been controversial, as the infection is often self-limiting.[29] However, studies have found that while treatment shows no effect on final visual acuity, antibiotic therapy can speed visual recovery.[29] In 1998 a retrospective case series evaluated seven cat-scratch neuroretinitis patients treated with oral doxycycline and rifampin and concluded that antibiotic treatment shortened the disease course.[29] This treatment regimen has since been adopted by, and published in, medical journals and textbooks.[29] A study in Japan isolated 32 strains of *B. henselae* to investigate antibiotic susceptibility. They found a high susceptibility to antibiotic treatment and concluded that macrolides and minocycline can be reliable options when treating CSD.[31] Another study found that compared to antibiotics alone, a combination of systemic antibiotics and corticosteroids was superior in treating moderate to severe infections.[29] In healthy individuals, neuroretinitis due to ocular CSD has a good prognosis with often complete or near-complete recovery.[30] However, contrast sensitivity, visual evoked potentials, and color vision may be subnormal or abnormal following severe disease.[30]

Other infectious and parasitic diseases should be considered in the differential diagnosis of a neuroretinitis etiology. In addition to previously mentioned viral conditions, bacterial agents including, tuberculosis, syphilis, Lyme borreliosis, leptospirosis, and rickettsiosis with parasitic infections including toxocariasis, toxoplasmosis, angiostrongyliasis, cysticercosis, gnathostomiasis, thelaziasis, and

trichinosis [15,16,17] should remain on the differential.

Lastly, there are other ocular conditions that may present with neuroretinitis which have unique characteristics that are worth mentioning. Diffuse unilateral subacute neuroretinitis (DUSN) is thought to be caused by helminths with intraocular worms visible in about 25% of cases.[15] DUSN typically presents more insidiously with severe vision loss, neuroretinitis, vitritis, and pigmented epithelial derangements, often in healthy young patients. Many patients present in later stages; the disease progresses to optic atrophy and narrowing of vessels if left untreated.[32] Another similar condition is Idiopathic Retinal Vasculitis and Aneurysms associated with Neuroretinitis (IRVAN) which presents with characteristic microaneurysms in arterioles. This is commonly found bilaterally in young, otherwise healthy females.[15]

Histologic proof of human nematode infection of the eye was made nearly 70 years ago and *Toxocara canis* and *Toxocara cati* were morphologically identified in humans.[33] Toxocariasis now represents the most prevalent of human helminthic infections in the industrialized world.[34,35] The roundworms are capable of producing thousands of eggs per day. The eggs are shed within the feces of infected animal hosts and have the ability to remain viable in the soil for several months or even years. If accidentally ingested by human hosts through poor hygiene practices or through consumption of raw meat from animals infected with larvae, the eggs can hatch in the human intestine and then enter the portal circulation.[36-38] Three types of toxocara infection syndromes are recognized including visceral larva migrans (VLM), covert toxocariasis (CT), and ocular toxocara (OT).[36,37]

Presenting systemic symptoms of VLM are varied and numerous often including fever and cough in the presence of elevated IgE levels. A severe systemic invasion, especially in children, may result in symptoms of fever, hepatosplenomegaly, pneumonitis, and convulsions. [18,34,36,39]

Covert toxocariasis (CT) results in more vague symptoms including coughing, sleep disturbances, abdominal pain, headaches, nausea, or cervical lymphadenitis.[36]

Ocular toxocariasis (OT) is the most common presentation and may manifest as endophthalmitis, chorioretinal granulomas, or neuroretinitis.[36,38] Symptomatic vision loss from OT stems from direct retinal damage from granuloma formation, the secondary effects of retina damage (edema, tractional bands, retinal detachments), and intraocular inflammation.[40,41] While ocular inflammation is often severe, ocular pain is rare and therefore, many cases of OT are found during routine examination.[42] Ocular complications result from an immune response to the presence of toxocara larvae in the eye. The most common ocular complication is

posterior pole and peripheral granulomas, while the most visually devastating is a tractional retinal detachment secondary to inflammatory fibrosis.[42] Importantly, the clinical observation of a migrating granuloma is pathognomonic for ocular toxocariasis.[40] Neuroretinitis from toxocara is a rarer presentation and has been reported in only 7.2% of all ocular toxocariasis cases.[43]

OCT associated findings specific to neuroretinitis may include the presence of vitreous cells and appearance of infiltrates on the optic nerve head which have been noted to precede the presence of macular star formation. Concentric ring patterns have been observed on the inner retina expanding outward from disc when using en face analysis on OCT at the vitreoretinal interface.[44]

About 5% of the US population, or 12 million people, test seropositive for toxocariasis.[35,41,45] These numbers may be even higher in rural areas [36] where infection rates remain higher in men, children, and minority ethnicities.[35,42] In some parts of the world there is a high prevalence of seropositivity for toxocara associated with the consumption of raw meat.[34,46]

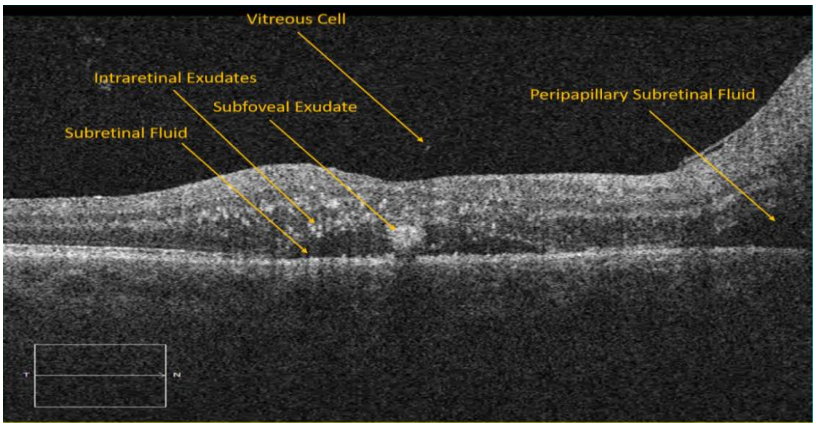

Figure 14: Descriptive OCT line scan of the right eye at the emergent visit

Definitive diagnosis of ocular toxocariasis can be made with direct observation of the presence of larvae in ocular tissue.[43] However, this is rare and diagnosis is typically made based on exposure history, clinical examination, and laboratory blood analysis including toxocara antibodies.[18,38] The recommended diagnostic testing sequence today for toxocariasis includes enzyme-linked immunosorbent assay (ELISA)[46-48] followed by immunoblot testing.[49] A newer assay testing for rTc-CTL-1 antigen to toxocara has shown 90% sensitivity and 99% specificity and may provide more reliable results.[35] The absence of serum antibodies does not necessarily exclude toxocariasis as a diagnosis as there have been reports of ocular toxocariasis in seronegative patients presumably due to low titer levels as the

infection is localized to the eye.[42,46] For our patient, the laboratory used the ELISA method for detecting toxocara antibodies, however, it did not subsequently order confirmatory immunoblot testing as suggested above.

Elevated IgE and eosinophilia are also common in helminthic infections. Some studies have used IgE elevation to support toxocariasis diagnosis following a positive Western Blot.[38] One study found that 17 out of 22 seropositive patients had elevated IgE serum levels.[43] It is estimated that toxocariasis infection has a prevalence of 80% in dogs aged between 2-6 months old and between 10-75% for cats.[34] A history of close contact with pets should be investigated in every OT patient, and if affirmative, these pets should be evaluated by a veterinarian.[50]

The decision to initiate treatment in a seropositive patient is made when there are symptoms and evidence of end organ damage. Currently, the treatment of choice is oral albendazole as it penetrates the gastrointestinal tract and crosses the blood brain barrier.[39]

Albendazole is an antiparasitic agent from the class of medications known as benzimidazoles.[51] It has a broad spectrum in the treatment of multiple helminthic infections [38,50] and the mechanism of action involves binding selectively to parasite tubulins preventing polymerization. Albendazole has a beneficial low likelihood for human toxicity.[36] Common side effects may include nausea, vomiting and stomach pain, and elevated liver enzymes. Side effects are generally short term and are typically tolerable.[51]

Steroids are used in the treatment of OT, since potential immunologic reactions resulting from dying larvae can cause damaging ocular inflammation.[36] Both topical and systemic corticosteroids are utilized to treat acute active inflammation associated with OT depending on its location and severity.[40] In contrast, when treating VLM (systemic toxocariasis), steroid alone treatment is dangerous as larvae migration may be enhanced.[36] In most instances of OT with active inflammation and positive serology, a combination treatment using albendazole and corticosteroids is used although some controversy exists with albendazole therapy due to a lack of randomized controlled trials.[36,40,46,48,49]

A retrospective cohort study by Ahn[46] in 2014 involving steroids and albendazole was completed to assess treatment outcomes for patients diagnosed with OT. A total of 101 adult patients were enrolled with nearly 70% of patients exhibiting elevated serum IgE levels. Patients were treated with medication or surgery depending on their retina status, symptoms, and level of inflammation. Those treated with medication received topical and/or oral corticosteroids (0.5-1mg/kg/day) depending on the presence and/or location of the ocular inflammation.

Additionally, if there was elevated serum IgE or eosinophilia, then oral albendazole 400mg bid P.O. x 2 weeks was added to the treatment regimen.

From this treatment stratification, four distinct groups emerged:

1. Steroid and albendazole therapy (inflammation and elevated IgE or eosinophilia)
2. Albendazole only (no inflammation but elevated IgE or eosinophilia)
3. Steroid only (inflammation only without elevated IgE or eosinophilia)
4. No treatment (no inflammation, no elevated IgE or eosinophilia)

Patients with follow-ups of greater than 3 months duration were monitored for recurrence and treatment outcomes to include best corrected visual acuity (BCVA) and level of inflammation. At 3 months, there were no significant changes in BCVA for any group, however the steroid treated groups had a significant reduction in ocular inflammation. In those groups with ocular inflammation there was no difference between the steroid only and steroid and albendazole treatment group in BVCA or inflammation. At the 6-month mark, the recurrence rate in the combined therapy group (steroid with albendazole) was significantly lower than the steroid only group. (17.4% vs 54.5%). There were no differences in recurrence in the eyes without inflammation groups (albendazole only vs untreated).[46]

In summary, although albendazole did not have an impact on improving BCVA outcomes, it seems that it may have a role in lowering the recurrence rate of OT in eyes demonstrating inflammation.[46]

Our patient's neuroretinitis treatment protocol was similar but not identical to the aforementioned study protocol. The similarity includes the combination therapy approach with the use of oral albendazole and oral steroids. The differences include the dose and duration of our treatment with the albendazole therapy (800 mg for 30 days). In contrast to the study results, the BCVA outcome was favorable for our patient. Additionally, our patient has experienced no recurrence of his OT. This case underscores the potential benefits of treating patients with OT using the combination therapy of albendazole with steroids, especially when the patient has pre-existing vision loss.

CONCLUSION

This case describes the diagnosis and treatment for the rare condition of neuroretinitis secondary to a toxocara infection. While cat scratch disease was

initially suspected, detailed laboratory testing identified the true, and more rare, causative infectious agent. A variety of differential diagnoses were ruled out through laboratory and imaging studies. Consultations with neuro-ophthalmology and infectious disease specialists were exceedingly valuable in contributing to a positive outcome for this patient. This patient's preexisting ODD with vision loss heightened the concern to preserve the patient's remaining vision and further added to the complexity of this challenging case. The importance of medical history questions regarding animal contact also proved vital for accurate diagnosis and treatment of this sight threatening condition.

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