Acute Central Vision Loss in an IV Drug User

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ABSTRACT

This report describes the case of a 21-year-old heroin user who presented with a 6-day history of decreased vision in her right eye, preceded by 1 week of headache and tender scalp nodules, neck stiffness, and photophobia. A broad infectious workup for acute vision loss was completed, and she was ultimately presumed to have acquired toxoplasmic chorioretinitis (ocular toxoplasmosis). We review the initial workup for chorioretinitis, and the epidemiology, diagnosis, and treatment of ocular toxoplasmosis. Intravenous drug users may be at increased risk of acquired ocular toxoplasmosis.

CASE PRESENTATION

A 21-year-old heroin user complained of 6 days of decreased vision in her right eye. Vision loss was preceded by 1 week of headache and tender scalp nodules, neck stiffness, and photophobia. On further review of systems, she had intermittent fevers and chills for the past 6 months that she attributed to withdrawal from heroin. Of note, she was actively still using heroin on a daily basis, with occasional marijuana and benzodiazepine use. She shared needles with her partner, with whom she was sexually active. She endorsed condom use for contraception.

Ophthalmic examination demonstrated counting fingers vision in the right eye and 20/20 vision in the left eye at near, normal intraocular pressures, and no evidence of inflammation in the anterior chambers. Dilated fundus examination demonstrated a 2 mm white chorioretinal lesion in the right eye involving the fovea with overlying vitritis. No lesion was seen initially in the left eye. The optic nerve was healthy as was the visualized periphery. There was no adjacent chorioretinal scar identified. She was admitted late in the evening on day 1, and her presenting exam was significant for nuchal rigidity, a positive Brudzinski's sign, numerous tender nodules on her scalp, and track marks on her upper extremities. She was afebrile and her vital signs were appropriate.

A urine pregnancy test was negative. Her white blood cell count was 10.1 with an absolute lymphocyte count of 3131. A lumbar puncture was attempted overnight but unsuccessful. Blood bacterial and fungal cultures were drawn, as well as a variety of fungal and parasite antibody tests including *Toxoplasma* serum IgM and IgG, *Histoplasma* serum antibody and urine antigen, and *Blastomycoses* urine antigen. She was treated empirically with voriconazole, vancomycin, and ceftriaxone. Ampicillin was also started due to concern for Listeria as we did not initially know the patient's HIV status. Rapid HIV testing was negative the following morning and HIV RNA was not detected. She was not checked for any other form of immunocompromise as she had no history of transplant or chronic steroid use and her initial blood counts were not indicative of a cell-mediated defect. Hepatitis labs were drawn because of her intravenous drug use, which showed immunity to hepatitis B and absence of hepatitis C RNA. She did have a successful lumbar puncture in interventional radiology on the morning of day 2. Cerebrospinal fluid (CSF) was clear and colorless and Gram stain revealed no organisms. Cell count and chemistries were atypical for meningitis. CSF culture was negative.

Although vitreous sampling would have been helpful diagnostically, it was not done because ophthalmic examination was stable with systemic therapy alone (Figure: A, B). Infectious disease was consulted, and ampicillin and ceftriaxone were switched to cefepime on day 3. A transthoracic echocardiogram for a possible septic embolic source was negative for vegetations. Magnetic Resonance Imaging (MRI) of the brain was also nega-

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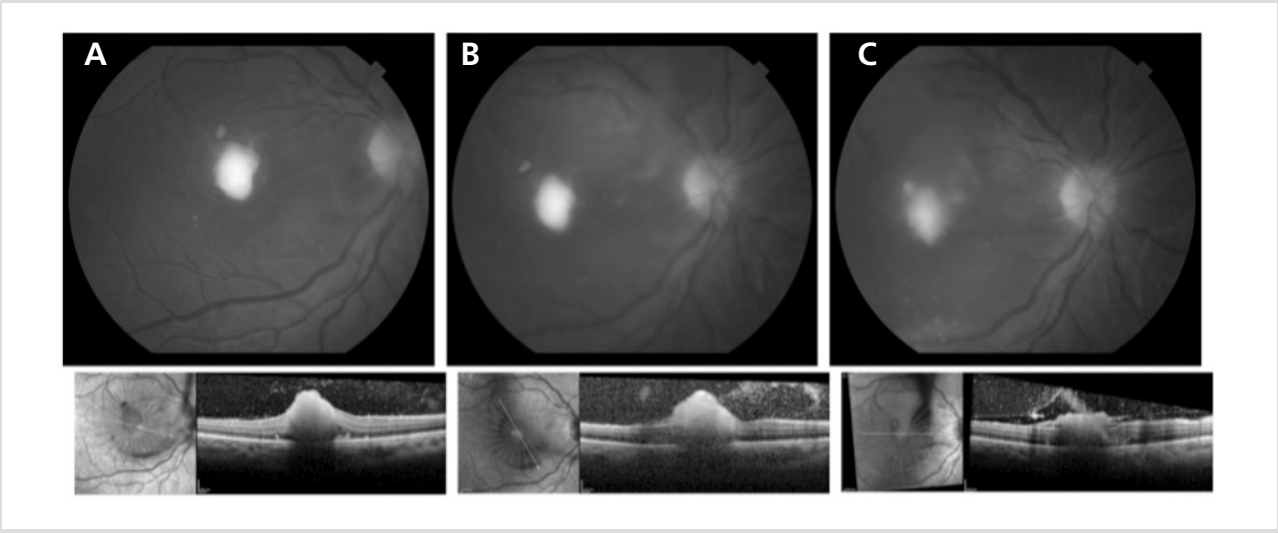
Figure. Progression of Patient's Ophthalmologic Exam



Fundoscopy and optical coherence tomography (OCT) images show patient's ophthalmologic exam on (a) day of admission; (b) 4 days after admission; (c) 2 weeks after admission.

tive. On day 4, *Toxoplasma* IgM returned positive (1.70 IU/ml, range 0.0-0.99 IU/ml), and IgG returned negative (< 0.2 IU/ml). Because of the association of acquired *Toxoplasma gondii* infection with cat exposure, further history was obtained from the patient, which did not reveal any significant feline exposure. She began treatment for acute toxoplasmic chorioretinitis with pyrimethamine, leucovorin, and sulfadiazine. Empiric antibacterials and antifungals were stopped on discharge (day 6), as her bacterial and fungal blood cultures were negative. Sulfadiazine was changed to clindamycin on discharge due to cost of medication. She was also prescribed a prednisone taper until follow up with ophthalmology.

On discharge, her scalp nodules had decreased in size and were no longer tender. They were thought to be lymphadenitis secondary to acute *Toxoplasma* infection. While we did not biopsy these lesions during her admission, this may have been a useful non-invasive way of ruling out a concomitant infection. Ophthalmic examination was slightly improved in the right eye over the ensuing couple of weeks with lesion involution (Figure C). However, a small area of chorioretinitis was apparent in the left macula as well. This remained stable and may have been missed on initial examinations. She was lost to follow-up 1 month after her initial presentation.

DISCUSSION

Toxoplasma gondii is believed to be the most common cause of chorioretinitis in the United States,[1] with ocular toxoplasmosis affecting nearly 1.26 million people.[2] While 22.5% of the adolescent and adult population in the United States are seropositive indicating prior exposure,[2,3] most such individuals never develop clinical symptoms.[4] Approximately 2% of seropositive individuals in the United States develop ocular toxoplasmosis.[3,4] Infection can occur through fecal-oral transmission, needle sharing, directly from a mother to a fetus during pregnancy or childbirth, and via contaminated blood transfusions.[5] Intravenous drug users represent an interesting at-risk group for development of ocular toxoplasmosis, as one mode of transmission of the parasite is via needle sharing with an infected individual. Because the viability of infectious tachyzoites does not drop until 6 to 12 hours after exposure to the extracellular environment,[6] transmission of the parasite via needle-sharing is an important consideration. In a Chinese study, the prevalence of *T gondii* in IV drug users ranges from 17.3% to 21.8%, significantly higher than the prevalence of drug users who do not use the intravenous route in that population (7.8%, $P < 0.01$).[5] In addition, duration of IV drug use correlated with seropositivity, as 21.8% of individuals with greater than 5 years of IV drug use tested seropositive compared to 8% of those with fewer than 5 years of IV drug use.[5]

While it was previously believed that the majority of cases of ocular toxoplasmosis in adolescent and adult patients were reactivated cases of infections acquired in utero,[7] it is now established that acquired infection is more common,[1-3] with nearly two-thirds of cases acquired postnatally.[4,8] In patients with reactivated infections of ocular toxoplasmosis, there may be a history of previous episodes of blurred vision related to episodic chorioretinal inflammation.[7] Toxoplasmic serological profiles can be used to help differentiate acute from chronic infection.

Risk factors for acute acquired *T gondii* infection include eat-

ing raw ground beef; rare lamb; locally produced cured, dried, or smoked meat; working with meat; drinking unpasteurized goat milk; and having 3 or more kittens.[2,7] Patients with acute acquired ocular toxoplasmosis have a more optimistic prognosis than those with reactivation of congenital disease.[1] The severity of disease also can be affected by the immune competence of the host, the age of the host (highest risk associated with extremes of age),[3] and the genotype of the strain.[4,9]

Clinical symptoms of ocular toxoplasmosis most commonly include floaters, blurred vision, or visual loss, usually without systemic signs.[4] If present, systemic signs can include cervical lymphadenopathy or mononucleosis-like infection.[4] Ophthalmic examination typically reveals a unilateral yellow-white necrotizing retinochoroiditis with fuzzy borders[4] associated with adjacent choroiditis, vasculitis, hemorrhage, and vitreitis.[9] The primary site of infection is the retina, but the choroid, vitreous, and anterior chamber are also involved.[9] The acute inflammatory phase typically resolves in weeks to months and leaves permanent white choroidal scars with clumps of dark pigment. Often there are lesions of different ages existing simultaneously.[7] An eye examination that is suspicious for infection with *T gondii* should also prompt consideration of other pathogens such as syphilis, tuberculosis, viral-induced necrotizing retinopathies, aspergillosis, or coccidiodomycosis,[4,7] in addition to non-infectious etiologies such as Behçet's disease, multifocal choroiditis and panuveitis, and serpiginous choroiditis.[4]

Following the initial clinical exam, serology should be obtained to help establish the diagnosis. Negative enzyme-linked immunosorbent assay (ELISA) serology can help exclude toxoplasmosis; however, positive serology does not necessarily confirm ocular infection. A patient with fundoscopic exam findings that are typical of ocular toxoplasmosis who is positive for *Toxoplasma*-specific IgG and negative for *Toxoplasma*-specific IgM who responds appropriately to anti-*Toxoplasma* therapy is considered to have a reactivated form of ocular toxoplasmosis.[10] However, a patient with the above exam findings who tests negative for *Toxoplasma*-specific IgG but positive for *Toxoplasma*-specific IgM is likely to have acute disease, and further testing with intraocular fluid is recommended, though not required, to make the diagnosis.[10] It is important to note that vitrectomy with aqueous humor analysis for *T gondii* DNA using PCR carries a significant risk of ocular morbidity including cataract, retinal tear or detachment and glaucoma or ocular hypotony post-operatively. The risk of morbidity is further increased when the eye is inflamed, as it was in the case scenario described above, which is why the test was not performed on our patient even though it could have provided diagnostic confirmation.

Treatment typically consists of pyrimethamine, sulfadiazine, folinic acid, and systemic corticosteroids. Folinic acid supplementation is added to help decrease the thrombocytopenia and leukopenia induced by pyrimethamine.[9] Therapy compliance can be an issue, as the traditional regimen is nearly 10 pills per day and it is necessary to monitor blood cell counts during treatment.[4] There are other alternatives to the classic regimen including a combination of clindamycin, pyrimethamine, and corticosteroids or a combination of trimethoprim-sulfamethoxazole and corticosteroids.[9] A typical course is at least 6 weeks. For patients with contraindications to systemic therapy, intravitreal injection of clindamycin and steroids may be of benefit.[4,9] While treatment helps to control the infection and inflammation, it will not prevent recurrence,[9] and recurrence rate after treatment is 5% to 30%.[7] Long-term intermittent treatment with trimethoprim-sulfamethoxazole has been shown to decrease recurrence rates from 23.8% to 6.6%.[11] It is unknown whether recurrence of ocular toxoplasmosis is due to reactivation of infected cells elsewhere in the body carried to the eye via immune cells, reactivation of infected cells within the eye, or due to acquisition of a new parasitic infection with hematogenous spread.[8]

The patient's IV drug use was an important consideration in her care. The patient followed up with ophthalmology initially, but not with the infectious disease department. In documented phone contact, she reported not being able to make appointments due to financial and transportation issues. We do not know if or how long she took her toxoplasmosis treatment.

While it is now known that acute acquired ocular toxoplasmosis is more common than reactivated infections acquired in utero, less is known about the link between IV drug use and *Toxoplasma* infection. The role of hematogenous spread and the in vitro survival of the parasite for 6 to 12 hours following exposure to the extracellular environment suggests that IV drug users may be at considerably higher risk of acquiring infection than the general population. As mentioned above, a Chinese review notes a higher prevalence of seropositivity in IV drug users compared to drug users who do not use the intravenous route,[5] but more research is needed. It is also important to determine if people who share needles with those who have symptomatic toxoplasmosis are at increased risk for infection and if these partners should receive prophylaxis. While our patient likely acquired the infection from needle sharing with her partner, he did not have evidence of symptomatic disease, so even if clear guidelines for prophylaxis are delineated through further research, it is unlikely our patient would have met criteria for prophylaxis. In addition, if recurrent infection is in fact caused by new entry of parasites into the blood stream as one theory suggests,[8] given the high prevalence of *T gondii* in the general population it may be reasonable to infer that IV drug users would be at much higher risk of reinfection. In a prospective randomized open-labeled interventional clinical

trial conducted in Brazil, investigators found that long-term intermittent treatment with trimethoprim-sulfamethoxazole can reduce recurrence rates from 23.8% to 6.6%.[11] It is unclear how this prophylactic regimen would apply to IV drug users; however, this is an area that warrants further research.

CONCLUSION

Acute vision loss in an IV drug user has a large differential diagnosis. Infectious causes are of greatest concern, including bacterial, fungal, and parasitic etiologies (See appendix online at www.wisconsinmedicalsociety.org/_WMS/publications/wmj/pdf/114/2/114no2_bettendorf_appendix.pdf). Such patients need to be treated broadly with antibacterial and antifungal agents until the diagnosis is confirmed. In addition to addressing the patient's acute vision loss, it is important to complete a full review of systems and a detailed physical exam to identify evidence that may help reach the diagnosis. Any critical findings such as this patient's meningismus must be addressed promptly as these findings may be life threatening. Acquired ocular toxoplasmosis is more common than previously thought and can be differentiated from reactivated congenital disease with *Toxoplasma*-specific IgG and IgM, as well as intraocular fluid sampling for *T gondii* DNA to confirm the diagnosis in select cases. Intravenous drug users who share needles may be at considerably higher risk of acquiring infection with *T gondii* compared to the general population, although further studies are needed to quantify this risk and determine if prophylaxis is warranted.

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Appendix. Differential Diagnosis of Chorioretinitis with Associated Symptoms, Clinical Findings and Diagnostic Procedures for Further Evaluation

Possible Diagnosis	Symptoms and Clinical Findings	Diagnostic Procedure
Toxoplasma gondii	Fundoscopic exam demonstrating necrotizing retinochoroiditis Lymphadenopathy Myalgias Encephalitis	Serum enzyme-linked immunosorbent assay (ELISA) serology (typical clinical presentation plus positive serum serology is sufficient to make diagnosis) Lymph node biopsy Ocular fluid cytology (helpful in patients with atypical presentation or those not responding to treatment)
Tuberculosis (TB)	Chronic cough Blood-tinged sputum Night sweats Weight loss Fevers Meningitis Back pain (with Pott's disease)	TB skin test TB Quantiferon Chest X-ray with cavitary lesions
Syphilis	*Primary:* Chancre *Secondary:* Maculopapular pink rash commonly involving palms and soles, condyloma latum, fever, malaise, weight loss, uveitis, optic neuritis *Tertiary:* Gummas, meningitis, tabes dorsalis, seizure, dementia, Argyll Robertson pupils, aortitis *Latent:* No findings *Congenital:* No findings or hepatosplenomegaly, fever, rash, neurologic changes, saddle nose deformity	Venereal disease research laboratory (VDRL) Rapid plasma reagin (RPR) Treponemal pallidum particle agglutination (TPHA) Fluorescent treponemal antibody absorption test (FTA-ABS) Direct fluorescent antibody testing using fluid obtained from a chancre Dark field microscopy of fluid obtained from a chancre
Brucellosis	Migratory arthralgias and myalgias Sweating	*Brucella* titer *Brucella* antibodies
Fungal eye disease	Central vision loss Ocular pain Photophobia Ocular injection Decreased or blurry vision Floaters Fundoscopic exam demonstrating iridocyclitis, iris granulomas, choroiditis, or chorioretinitis	Aqueous humor staining and fungal culture *Histoplasma* serum antibody *Histoplasma* urine antigen Coccidiodes serum antibody Serum galactomannan antigen assay (Aspergillus) Serum Beta-D-glucan assay (Aspergillus) Chest x-ray with nodules often in upper lobes
Sarcoidosis	Fatigue Weight loss Arthralgias Arthritis Dry eyes Blurry vision Shortness of breath Cough Rashes ranging from erythema nodosum to subcutaneous nodules to lupus pernio Uveitis Facial nerve palsy	Chest x-ray with mediastinal and hilar lymphadenopathy and variety of parenchymal features including reticulonodular opacities, and airspace-like opacities, fibrosis Non-caseating granulomas on biopsy Angiotensin-converting enzyme (ACE)
Viral induced necrotizing retinopathies	Periorbital vesicular rash in dermatomal distribution (not in CMV) Vision loss Floaters Visual field deficits Eye pain (not in CMV) Blepharitis Conjunctival injection Oculomotor palsies Ophthalmic exam with uveitis, retinal necrosis, keratitis, episcleritis, scleritis, or optic neuritis	Aqueous humor varicella, herpes simplex, cytomegalovirus DNA polymerase chain reaction (PCR)
Behçet's disease	Recurrent painful oral ulcers Recurrent painful genital ulcers Vision loss or decreased visual acuity Floaters Visual field defects Eye pain Conjunctival injection Ophthalmic exam with uveitis, retinal vasculitis, or papilledema Abdominal pain Pleuritis Cough Arthralgias Chronic meningoencephalitis Aseptic meningitis Skin lesions (acneiform nodules, erythema nodosum, pseudofolliculitis, papulopustular lesions) Positive pathergy reaction (hyper-reactivity of skin to minor trauma)	Diagnosis of exclusion, no specific testing available ESR and CRP may be elevated
Multifocal choroiditis and Panuveitis (MCP)	Photopsias Blurry vision Floaters Mild eye pain Enlarged blind spot Ophthalmic exam with anterior uveitis, vitritis, or chorioretinal lesions Fluorescein angiography with active lesions demonstrating early hypofluorescence with late hyperfluorescence	Diagnosis of exclusion, no specific testing available
Serpiginous choroiditis	Visual field loss Metamorphopsia Blurry vision Central scotoma Ophthalmic exam with subretinal infiltrates Fluorescein angiography with early hypofluorescence with late leakage Indocyanine green angiography with hypofluorescent areas from early to late frames Fundus autofluorescence of active lesions shows early hypofluorescence, with later blurred hyperfluorescence	Diagnosis of exclusion, no specific testing available

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