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Case report

A delayed diagnosis of ocular toxocariasis presenting as total monocular retinal detachment in an immunocompetent 57-year-old male

this parasitic infection.

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ARTICLE INFO	A B S T R A C T
<i>Keywords:</i> Toxocara canis Ocular toxocariasis Zoonotic Disease Infectious disease	A healthy 57-year-old man present to outpatient ophthalmological services in southwestern Connecticut with a 16-month history of unilateral periorbital pain, photophobia, and progressively decreasing visual acuity in his left eye. Prior extensive work-up for uveitis in his home state of Mississippi had yielded no etiology for his symptoms, and empiric therapy with glucocorticoid eye drops had not halted their decline. Fundoscopic examination demonstrated total combined retinal detachment of the left eye. Extensive repeat serological and immunological screening was positive for Toxocara immunoglobulin-G, consistent with a diagnosis of ocular toxocariasis, and the patient completed a course of albendazole with stabilization of symptoms. Despite <i>toxocara</i> being endemic to the United States, diagnoses of ocular toxocariasis are extremely uncommon, with the majority of cases occurring in young children. This unusual case of ocular toxocariasis in a healthy adult serves to illustrate that significant, irreversible morbidity can result from lack of both clinician and public awareness of

Introduction

Ocular Toxocariasis (OT, previously Ocular Larva Migrans) is an uncommon, yet distinct clinical manifestation of infection by larval form of either Toxocara canis or Toxocara cati. These zoonotic nematodes are endemic across the United States and can be transmitted to humans via ingestion of embryonated eggs released from the intestinal tract of dogs and cats, which serve as the definitive hosts for the two parasite species, respectively. Once ingested by humans these larvae invade the intestinal mucosa and enter the bloodstream, from where they can migrate throughout the body. In OT, invasion by larvae into the posterior segment of the eye results in local inflammation, retinal granuloma formation, and fibrosis - all of which can result in partial or complete vision loss. OT most commonly occurs in children under 10 years of age, as they are more likely to come into close contact with contaminated soil or sand [1]. However, despite being one of the most prevalent zoonotic infections worldwide, lack of clinical suspicion for OT in adults can result in delayed diagnosis and often permanent vision loss [2]. Here we present a case of delayed diagnosis of ocular toxocariasis in a healthy 57-year-old man presenting with total monocular retinal detachment.

Case presentation

A 57-year-old male originally presented to outpatient ophthalmological services at a tertiary care center in southwestern Connecticut for a second opinion regarding left eye visual blurring. He reported a 16month history of progressive deterioration of visual acuity (VA) in his left eye, associated with intermittent ipsilateral periorbital pain, photophobia, and headaches.

Over the preceding year he had sought consultations with multiple ophthalmological specialists across the southeastern United States, and had received a diagnosis of unilateral uveitis with total retinal detachment of the left eye 11-months prior to assessment. He reported that prior laboratory work-up had not yielded an etiology for his uveitis, and that he had been commenced on twice-daily glucocorticoid eye drops for symptomatic management.

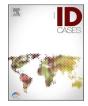
The patient was a military veteran permanently residing in rural Mississippi, where he lived alone. He had previously worked in a factory with heavy machinery but had recently become unemployed. His past medical history was significant only for chronic lower extremity deep vein thrombosis (DVT) on apixaban, migraines, and peripheral venous insufficiency. He had previously smoked half a pack of cigarettes daily but had quit over a year prior to symptom-onset. He did not drink

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alcohol. Significantly it was noted that he lived with multiple dogs and cats which he had taken in as strays, including young puppies, but reported no other animal or livestock exposures. He denied any dietary preference for offal or undercooked/raw meat products.

Investigations

At the time of assessment, the patient reported persistent left eye vision blurring and periorbital pain, with intermittent photophobia. He continued to report intermittent severe, global headaches every 1-2 weeks, which were more frequent than his prior migraines. He reported no improvement in symptoms with the glucocorticoid drops. He denied symptoms in the contralateral eye, and systemic review was otherwise negative. Gross extraocular examination was unremarkable bilaterally. Pupil examination demonstrated sluggish left pupillary response to light with an ipsilateral relative afferent pupillary defect (RAPD). VA was 20/ 20 in right eye, with only hand motion detectable in the left eye. Left eye fundus examination (Fig. 1) was significant for total combined retinal detachment, with extensive subretinal fibrosis and exudates. Fluorescein angiography demonstrated evidence of temporal ischemia and subsequent neovascularization. B-scan ultrasonography again confirmed retinal detachment (Fig. 2) but was not suggestive of masses or granuloma formation. Examination of the right eye fundus demonstrated only benign asteroid hyalosis.

A repeat workup for uveitis was obtained; complete blood count (CBC), comprehensive metabolic panel (CMP), erythrocyte sedimentation rate (ESR), and c-reactive protein (CRP) were all within normal limits. Of note peripheral eosinophil count was normal at $0.3 \times 1000/\mu$ l. Immunological screening was weakly positive for anti-nuclear antibodies (ANA) on indirect immunofluorescence (1:80, speckled pattern), but was negative for rheumatoid factor (RF) and antineutrophil cytoplasmic antibodies (ANCA). Serum angiotensin-converting enzyme (ACE) and lysozyme levels were also within normal limits. Serological testing yielded negative results for Lyme disease, Toxoplasmosis, and Treponemal antibodies, human immunodeficiency viruses (HIV) 1 and 2, but was positive for Toxocara immunoglobulin-G (IgG). A chest x-ray was unremarkable.

Given the positive Toxocara serology and significant history of exposure to stray dogs and cats, the patient's overall clinical picture was highly consistent with ocular toxocariasis. He was therefore referred for outpatient Infectious Diseases consultation, where magnetic resonance imaging (MRI) and neurology referral were recommended to exclude concomitant neurotoxocariasis, given his history of progressive

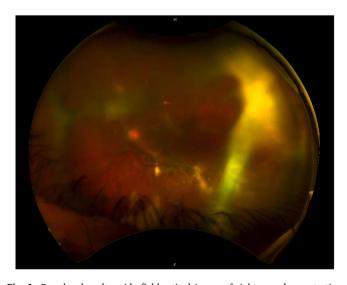


Fig. 1. Pseudocolor ultrawide field retinal image of right eye, demonstrating extensive vitreous opacifications.

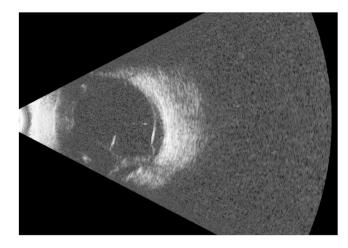


Fig. 2. B-scan ultrasound image of right eye, demonstrating retinal detachment.

headaches. Subsequent MRI brain only demonstrated mild white matter changes consistent with chronic ischemia. Following neurological consultation, it was felt that his headaches were most likely consistent with migraines, and that urgent invasive investigations to further exclude cerebral toxocariasis were not warranted at that time. The patient was provided with a prescription of sumatriptan for breakthrough headaches.

Prior to further planned follow-up, the patient was admitted to a local community hospital with an acute-on-chronic exacerbation of his right lower extremity DVT, likely secondary to poor oral medication compliance, and was placed on a therapeutic low molecular weight heparin (LMWH) infusion. An inpatient Infectious Disease consult was requested as part of his ongoing OT workup. As he was placed on bridging anticoagulation at that time, the opportunity was taken to perform a lumbar puncture (LP) to more definitively exclude neuro-toxocariasis. Cerebrospinal fluid (CSF) analysis yielded normal glucose and protein concentrations, and was negative for leukocytosis. Concurrent serum tests demonstrated normal peripheral eosinophil and immunoglobulin-E (IgE) levels. Given these results it was felt that concomitant systemic or neurotoxocariasis were unlikely.

Treatment

The patient was informed of the investigative results, and the likely diagnosis of ocular toxocariasis. Given the severity and duration of the retinal detachment, it was unlikely that any antimicrobial or ophthalmological intervention would yield improvement in his left eye vision. However, it was reasoned that a course of antihelminthic therapy would be advisable to prevent subsequent involvement of the healthy right eye. He was therefore commenced on albendazole 400 mg two times per day for a total of 14 days. After a 7-day hospital admission he was discharged on his prior dose of apixaban, with outpatient follow-up arranged with infectious disease, ophthalmology, hematology, and primary care.

Outcome and follow-up

The patient was seen by infectious disease and ophthalmology for follow-up of his OT. He tolerated and completed his course of albendazole without issue. He reported further mild decrease in left eye visual acuity and intermittent ongoing periorbital pain in the intervening 3 months, but no issues with his right eye. Slit lamp examination demonstrated interval development of left cataract, but otherwise overall stable appearances of both eyes. Follow-up CBC remained negative for eosinophilia. He has further follow-up arranged with ophthalmology for aqueous humor sampling for toxocara polymerase chain reaction (PCR).

Discussion

Although toxocariasis remains relatively unknown to both the general public and many clinicians, it is one of the most common zoonotic parasitic infections worldwide, and is endemic to the United States [3]. A national cross-sectional survey of the US published by the CDC in 2008 demonstrated a toxocara antibody seroprevalence of 13.9 % across a representative sample of over 20,000 individuals, with higher rates of seropositivity being associated with lower household income and lower levels of education [4]. Despite this high seroprevalence, incidence rates of OT remain incongruously low; only 68 individuals across the United States received a new diagnosis over a recent 12-month period, with the median age at diagnosis being 8.5 years, and 68 % of patients subsequently suffering permanent vision loss [1]. Here we present a case of delayed diagnosis of ocular toxocariasis in an immunocompetent 57-year-old man, resulting in significant irreversible visual impairment in the affected eye. Despite OT predominantly being a disease of childhood, it should be always be considered as a differential in adults presenting with new visual impairment.

We performed a literature review of case reports of OT in adults published in the past 20 years, all of which serve to highlight certain key points in clinical history and laboratory findings which can expedite diagnosis. Across the 12 cases analyzed, ages ranged from 17 to 68years-old at the time of presentation, with the majority (75 %) presenting with unilateral symptoms. 6 cases reported regular contact with either domesticated or stray dogs, and 2 others reported either regular or recent ingestion of raw meat/offal. All cases presented with some form of visual disturbance, either reduced visual acuity or significant increase in intraocular floaters, though only 5 cases reported associated uveitic symptoms of pain or redness. The most common finding on fundoscopy was retinal granuloma formation (83.3%), with two cases presenting with retinal detachment. Interestingly, of the 11 cases who underwent serological screening 10 were seropositive for Toxocara IgG. 5 cases underwent ELISA testing of intraocular samples, all of which were positive for Toxocara IgG, including the one case with negative serology [5-16].

Toxocara canis and *Toxocara cati* are species of roundworms for whom the definitive hosts are domestic dogs and cats, respectively. Transmission to humans usually occurs when embryonated eggs shed in animal feces are inadvertently ingested following contact with contaminated soil, or through larvae present in undercooked meat from paratenic hosts. Children are typically at highest risk of infection due to close contact with soil and sandboxes in playgrounds, compounded by lack of hygiene awareness. Once inside the gastrointestinal tract, embryonated eggs hatch into larvae, which burrow through the wall of the small intestine and disseminate throughout the body via the bloodstream. The two most well-described clinical syndromes resulting from *Toxocara* infection are Systemic Toxocariasis, usually characterized by pulmonary, hepatic, and central nervous system (CNS) involvement, and Ocular Toxocariasis, in which larval migration is restricted to the posterior segment of the eye and optic nerve [2,17].

OT typically affects older children and adolescents aged 8–16 years, and usually presents with unilateral visual blurring or vision loss. The most common form is characterized by development of subretinal or intraretinal granulomata within the posterior segment of the eye, with varying degrees of associated membranous and pigmentary changes. Additionally, some cases develop acute intraocular inflammation denoting nematode endophthalmitis/panuveitis, and present with eye pain, photophobia, and/or redness. With or without inflammation, development of tears or tractional forces on the retina can eventually lead to partial or total retinal detachment [2,17].

Diagnosis of OT is primarily based on clinical history and findings on fundoscopy, as leukocytosis and eosinophilia are not typically present in this localized form of infection. Diagnosis may be supported by serological testing through enzyme-linked immunosorbent assay (ELISA) detection of *toxocara*-specific IgG; however, whilst the reliability of such testing is relatively high in systemic *toxocara* infection (sensitivity and specificity 78 % and 92 %, respectively), its sensitivity is thought to be significantly lower in OT [3,18]. Direct sampling of aqueous humor may yield positive antibody titers in cases with negative serology but is often considered unnecessarily invasive to establish a diagnosis. If not already consulted, prompt referrals to Ophthalmology and Infectious Disease should be made following diagnosis.

The mainstay of medical therapy in OT involves topical or systemic corticosteroids to control intraocular inflammation and minimize complications. The precise role of antihelminthic therapy in ocular disease is not well-defined, due to limited studies into the intraocular pharmaco-kinetics and pharmacodynamics of such drugs; however standard treatment of albendazole 400 mg twice daily for 14 days has been shown to reduce recurrence rates in OT, in combination with steroid therapy [2, 19]. Additional surgical intervention may be considered for structural retinal complications of infection, such as retinal detachment or vitreous opacification, to attempt to either stabilize or improve visual acuity.

Here we present an unusual case of ocular toxocariasis diagnosed in a healthy adult man. Diagnostic delay through lack of clinician and public awareness of this parasitic infection may result in significant morbidity through profound and irreversible vision loss, as seen in this case. Although typically considered a pediatric disease, providers should always consider serological screening for toxocara in adults patients presenting with uveitic symptoms, particularly those with regular or recent exposure to untreated dogs or cats. Following diagnosis, prompt referral to both infectious disease and ophthalmological surgery is essential to minimizing poor patient outcomes and potential lifelong disability.

CRediT authorship contribution statement

George William Jowsey: Conceptualization, Data curation, Writing – original draft. **Gavin Xavier McLeod:** Investigation, Writing – review & editing.

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Ethical approval

Our Institutional Review Board (IRB) does not require formal IRB review or approval for case reports.

Consent

Written informed consent was obtained from the patient for publication of this case report. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Conflicts of interest

The authors have no conflicts of interest to disclose.

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