Rapid Therapeutic Response of Eosinophilic Meningoencephalitis in a Toddler With *Baylisascaris procyonis* Infection

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ABSTRACT

Introduction: Eosinophilic meningitis is an infrequently encountered condition. *Baylisascaris procyonis* (raccoon roundworm) infection, rarely diagnosed in North America, is a known cause of eosinophilic meningitis, often producing death or permanent neurologic damage.

Case Report: We recently encountered a toddler with geophagia and probable exposure to raccoon feces, who presented with eosinophilic meningitis and encephalitis, and was diagnosed with *B procyonis* infection and possible Toxocara co-infection. His marked peripheral eosinophilia and neurologic symptoms rapidly responded to corticosteroid and albendazole therapy.

Discussion: Since *B procyonis* infection is infrequently encountered, its diagnosis in the proper clinical and epidemiologic setting may not always be considered, resulting in a delay of appropriate therapy. Our patient, diagnosed and treated early in his course, demonstrated rapid clinical and laboratory improvement with anti-inflammatory and antiparasitic therapy.

Conclusion: In cases of eosinophilic meningitis, infection with *B procyonis* should be routinely considered to allow timely institution of effective therapy for this unusual but potentially fatal or debilitating infection.

INTRODUCTION

Eosinophilic meningitis is a rarely encountered condition in North American children.[1,2] We recently treated a toddler with eosinophilic meningitis and encephalitis who was diagnosed with infection with the raccoon roundworm *Baylisascaris procyonis (B procyonis). B procyonis* infection often produces death or permanent neurologic damage in affected individuals.[3-7] Because the infection is encountered infrequently, its diagnosis may not be considered and appropriate therapy may be delayed. Our patient, diagnosed and treated early in his course, demonstrated rapid clinical and radiologic improvement.

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CASE REPORT

A previously healthy 2-year-old boy presented with hyperacusis, confusion, and headache of 1 week's duration. He became sleepy, difficult to arouse, disoriented, and confused 48 hours prior to admission. He would not answer questions, had episodes of incontinence, and became ataxic. The child lived in a suburban area near Milwaukee, Wisconsin, with travel only in Wisconsin and to Illinois. He did have geophagia and had been observed eating dirt from a flower pot on his home's front porch.

On admission, the patient was afebrile with mild tachypnea. He was listless but could answer simple questions, such as stating his name. He had a normal neurologic exam without meningismus. A noncontrast computed tomography (CT) of his head and neck was normal. His peripheral white blood cell (WBC) was 15,000/μL with 23% eosinophils. Lumbar puncture opening pressure was 14cm. Cerebrospinal fluid (CSF) analysis revealed a glucose of 48mg/dL, protein 25mg/dL, and WBC of 132/μL with 70% eosinophils, 18% monocytes, and 11% lymphocytes.

Brain magnetic resonance imaging (MRI) was performed, demonstrating abnormal mildly enhancing periventricular and deep cerebellar white matter long repetition time (TR) signal hyperintensities bilaterally. Areas of mild nonenhancing long TR hyperintensity also were noted within the anteromedial aspects of the thalamus. Acute infarct, hemorrhage, and mass effect were not present. His ventricles were normal, without leptomeningeal enhancement or restricted diffusion. With the history of CSF eosinophilia, peripheral eosinophilia, and periventricular TR hyperintensity with subtle enhancement of hyperintense white matter, raccoon roundworm infection was strongly considered in a differential diagnosis that also included vasculitis, malignancy, and idiopathic hypereosinophilic syndrome.

Expanded history revealed that the patient's neighbors had seen raccoons in the patient's garage and around his home, including

the front porch where the flower pots were located. The child also had visited family in a more rural area, where he had potentially been exposed to dog and raccoon feces.

Shortly after admission, the child developed a left-sided facial palsy, dysmetria, and lagopthalmos. A dilated ophthalmic exam was normal. On hospital day 15, *B procyonis* serum serology from the Centers for Disease Control and Prevention (CDC) returned as positive. Simultaneously obtained CSF sent to the CDC was nonreactive. *Toxocara spp* serum serology sent to Quest Diagnostics (San Juan Capistrano, CA) also returned positive. Our patient was then treated with enteral albendazole, 200 mg twice daily for 4 weeks. He also received a 5-day course of intravenous methylprednisolone 30 mg/kg, followed by a 5-week oral steroid wean. Within 48 hours of starting therapy, his peripheral eosinophil count fell to 0 eosinophils/μL and his headaches improved.

Following discharge, the patient continued to recover clinically. Repeat serologic testing at 2 and 6 weeks for both *B procyonis* and *Toxocara spp* remained positive. A repeat MRI of the brain revealed persisting mild periventricular long TR hyperintensity, but no longer demonstrated the focal enhancement and tiny cystic foci previously noted. The child's parents reported complete resolution of his left facial palsy, gait abnormality, and speech problems 4 months after infection. A mild tremor with fine motor activities persisted.

DISCUSSION

Eosinophilic meningitis is defined as the presence of greater than 10% eosinophilia in the CSF.[1] Eosinophilic meningitis is a rare complication of a variety of conditions, including fungal, bacterial, viral, and parasitic infections, and can be associated with the presence of foreign bodies, malignancies, and medications.[2] Parasitic infections are particularly likely in the presence of concomitant peripheral eosinophilia.[2]

The 4 most common parasitic etiologies of eosinophilic meningitis include infection with *Angiostrongylus cantonensis, Gnathostoma spinigerum, Toxocara canis (T canis)* and *B procyonis*. Human infections with these zoonotic agents are generally restricted to tropical climates except for *T canis* and *B procyonis* infections, which also occur in temperate climates, including the Midwestern United States.[3,5]

During the life cycle of *B procyonis*, adult worms reside in the small intestine of the raccoon host, and eggs laid by female worms are shed in feces. Infected adult raccoons excrete millions of eggs daily in feces deposited in communal sites called latrines.[4] The eggs are resilient and remain viable for many years, even after exposure to harsh environmental conditions.[5,6] The infectious dose of *B procyonis* is low and has been estimated to be fewer than or equal to 5,000 eggs.[4,5]

Despite reports of *B procyonis* encephalitis, *B procyonis* is not considered a neurotropic agent. Only 5% to 7% of the total body burden of larvae migrate to the central nervous system (CNS) and ocular tissues. CNS infection is considered random, the result of nondirected migration of the parasites.[4]

The prevalence of human infection is currently unknown but may be higher than current estimates, given the potential for asymptomatic infection.[4] It is believed that the severity of the clinical manifestations is related to the number of eggs ingested.

Humans and other mammals become infected with *B procyonis* by ingesting contaminated organic materials or raccoon feces containing viable *B procyonis* eggs.[4-6] Young children, especially those 2 years and younger, are at increased risk for infection due to behaviors such as pica, geophagia, and placing contaminated objects in their mouths.[5] It is critical all children be excluded from areas potentially contaminated with raccoon feces such as raccoon latrines, to avoid contamination with and later ingestion of infectious *B procyonis* eggs. Other groups at increased risk for *B procyonis* infection include wildlife and zoo workers, animal damage and control workers, agricultural workers, trappers, hunters, and other individuals with increased exposure to raccoon latrines.[4] The risk of *B procyonis* infection is sufficiently high that after a suspected enteral exposure to raccoon feces, a 10-day "preventive" course of an antihelminthic be considered, even prior to the onset of clinical symptomatology.[4]

B procyonis infection should be suspected in the setting of xanthochromic CSF with eosinophilia. Definitive diagnosis is made through serologic testing of blood or CSF. Fecal examination for ova or adult parasites is not useful. Brain MRI of symptomatic patients typically shows subcortical nodular enhancement hyperintensities in the cerebellar white matter.[7]

T canis (dog roundworm) CNS infection should also be considered in patients with CSF pleocytosis and eosinophilia who demonstrate transient oligoclonal immunoglobulin bands in the CSF and peripheral eosinophilia with positive Toxocara serologies.[3] MRI in such patients typically shows cerebral lesions in cortical and subcortical regions and the centrum semiovale. A head CT may show hyperdense signals indicating calcification.[3] This pattern was not observed in our patient, nor was the typical ocular retinitis of toxocariasis seen.

Both *Toxacara spp* and *B procyonis* infections are most common in rural settings and where there is animal contact (cats and dogs or raccoons, respectively), geophagia, and dementia. Given the similar presentations of *T canis* and *B procyonis* infection, differentiation between these 2 infections formerly required the histologic identification of larva from brain biopsy. The invasive nature and lack of sensitivity of this method has been supplanted by more definitive serologic methods of diagnosis.

Initially, both *B procyonis* and *Toxocara spp* infections were detected using excretory secretor (ES) antigen ELISA. Both these ELISAs showed cross reactivity with one another[8] and *Toxocara spp* ES ELISA demonstrated cross reactivity with a variety of other parasites as well.[9,10] Components of *B procyonis* ES antigens have now been developed that are specific for that agent.[9,11] While the original *B procyonis* ES ELISA cross-reacted with *Toxocara spp* infections at rates as high as 90.6%,[12] recombinant synthesis of a

B procyonis antigen (BpRAG1) has improved specificity such that when used in a Western blot assay, test specificity for *B procyonis* now approaches 100%.[13] Currently, the CDC uses the BpRAG1 Western blot to identify *B procyonis* infection,[13,14] essentially excluding cross-reactivity with Toxocara infection.

Our patient had multiple positive *B procyonis* serologies. Given the extremely high specificity of the CDC assay, the patient's positive *B procyonis* serology indicates a true *B procyonis* infection. Based on the currently available information, this patient appears to be the first confirmed case of *B procyonis* infection in Wisconsin (J. Kazmierczak, Wisconsin State Department of Hygiene, oral communication, May 8, 2017).

Based on the multiple positive Toxocara serologies in our patient, a false positive *Toxocara spp* assay cannot be excluded, as cross reactivity of the current *Toxocara spp* assay against *B procyonis* infection is unknown. Other cases of apparent *B procyonis* encephalitis have been reported in which Toxocara serologies were presumed to be falsely positive.[15] However, co-infection with both parasites is possible, given this child's exposure to both raccoon and dog feces, and the fact that dogs can be co-infected with both *T canis* and *B procyonis*. Our patient lacks the typical MRI pattern seen in cerebral toxocariasis as well as retinal findings typical of toxocariasis. Our patient was treated with albendazole, which is effective for both parasitic infections.

Neural larva migrans (NLM) due to *B procyonis* infection has been frequently associated with severe, often fatal outcome.[5] Serious neurologic manifestations may result from larval migration through the central nervous system.[6] Larvae continue to grow during migration, inducing significant inflammation and increasing the damage.[6] Between 1981 and 2002, there were only 12 reported cases of *B procyonis* encephalitis.[16] Most diagnoses were established in that era by brain biopsy or at autopsy. It was estimated at the time that 46% of confirmed or probable neurologic infections with *B procyonis* were fatal, while the remaining nonfatal infections resulted in permanent, severe neurologic deficits.[6]

With wider availability of serologic testing, greater numbers of milder cases of *B procyonis* infection are being recognized.[5] The overall prevalence of human infections with *B procyonis* has increased and the spectrum of clinical disease has broadened.[4] Our patient had relatively mild clinical disease compared to most of the early cases in the literature, perhaps related to the ingestion of a relatively small number of eggs.

Given the high prevalence of *B procyonis* in the raccoon population and abundance of raccoons living near human dwellings, it seems likely that asymptomatic infections may occur. The prevalence of asymptomatic human infections, long-term consequences of such infections, and investigation into potential individual risk factors for more severe infections are areas for future investigation. The likely wide spectrum of clinical pictures emphasizes the importance of the consideration of *B procyonis* infection in any patient presenting with unexplained eosinophilic meningitis and neurologic symptoms, particularly since potentially effective therapy exists for such infection.

CONCLUSION

In cases of unexplained eosinophilic meningitis, infection with *B procyonis* should be considered to allow timely institution of effective therapy for this potentially fatal or debilitating infection.

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