Clinical Reasoning: A 12-Month-Old Male Child With Staring Episodes, Ataxia, and Right-sided Weakness

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Abstract

Baylisascaris procyonis, or raccoon roundworm, is a rare cause of eosinophilic meningoencephalitis with historically poor clinical outcomes. Symptoms of neural larval migrans begin approximately 2–4 weeks after ingestion with fatigue, nausea, fever, and lethargy and then rapidly progress to weakness, incoordination, ataxia, seizures, altered mental status, and finally coma. Only 31 other cases of CNS *Baylisascaris* neural larval migrans have been reported, with more than 25% being lethal. Of the remaining cases, all but 3 were neurologically devastated largely because of delays in diagnosis and treatment. We present a case of an infant with *Baylisascaris* neural larval migrans manifested as right hemiparesis, ataxia, and cortical blindness. Eosinophilia was missed at an outside hospital due to misidentification of eosinophils as monocytes on automated cell differential. Repeated testing of serum and CSF revealed marked eosinophilia consistent with eosinophilic meningoencephalitis, and serum antibody testing through the Centers of Disease Control confirmed *Baylisascaris* infection. Notably, this child had a remarkably positive outcome with near complete recovery of neurologic function after treatment with albendazole and steroids. Although eosinophilic meningoencephalitis is rare, accounting for less than 3% of all lumbar punctures with pleocytosis, this case illustrates (1) the importance of early disease recognition and treatment to improve patient outcomes and (2) the fact that automated cell differentials may misidentify eosinophils as monocytes.

Glossary

Section 1

A 12-month-old full-term, previously healthy, and typically developing boy presented to a community hospital with new-onset focal motor seizure (right-sided shaking and unresponsiveness) with secondary generalization, in the setting of congestion and tactile fevers. The seizure self-resolved after 30 minutes. On arrival to an outside Emergency Department, he was lethargic but had reportedly intact cranial nerves and symmetric localization to painful stimuli. A basic metabolic panel was unremarkable. His complete blood count (CBC) demonstrated a leukocytosis of 32,000 cells/μL (27% neutrophils, 48% lymphocytes, and 1% bands). A noncontrast CT of the head was normal. Lumbar puncture (LP) demonstrated 14 CSF red blood cells (RBC), 303 white blood cells (WBC; 30% neutrophils, 43% lymphocytes, and 27% monocytes), protein of 41 mg/dL, and glucose of 73 mg/dL. Nasopharyngeal swab testing for SARS-CoV-2 was negative. He was empirically treated with vancomycin and ceftriaxone given concern for bacterial meningitis until CSF cultures were negative at 48 hours. He remained afebrile and seizure-free and was discharged 2 days later with a reportedly normal neurologic examination and a presumptive diagnosis of viral meningitis.

Shortly after discharge, he developed new clusters of staring episodes lasting 1–2 minutes each and decreased use of his right arm. He was also reaching indiscriminately, as if trying to grasp objects that did not exist and, therefore, presented to our institution 12 hours after initial discharge. He was afebrile without meningismus, alert, but irritable. Pupils were equal, round, and reactive to light, but he did not fixate on faces, had no light aversion, and could not track. Facial movements were symmetric with crying, although he had no other vocalizations (baseline babbling with single words). He had significant axial hypotonia requiring left truncal support to sit. Right upper extremity movements were at least antigravity with a raking grasp, prominent tremor, and dysmetria. Left upper extremity and bilateral lower extremity strength was grossly normal. Sensation was normal. Deep tendon reflexes were 2+ except at bilateral ankles which were 4+ with 2–3 beats of clonus. Plantar responses were extensor bilaterally.

Questions for Consideration:

1. What is the differential diagnosis?
2. What are the next steps in diagnostic evaluation?

Figure 1 Neuroimaging Findings at Presentation
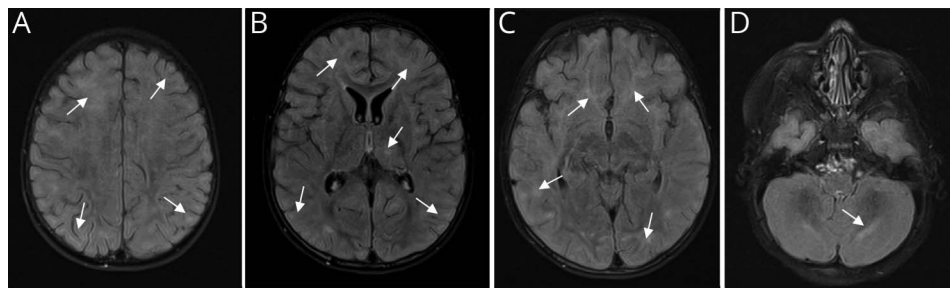
MRI brain demonstrating multifocal areas of T2/FLAIR signal intensity (white arrows) involving the (A) right greater than left frontal lobe and bilateral parietal lobes, (B) left greater than right thalamus, (C) bilateral temporal lobes and left occipital lobe as well as the splenium of the corpus callosum (not shown), and (D) the cerebellum.

Section 2

In a child with new abnormal movements concerning for seizure and progressive multifocal neurologic deficits, the differential diagnosis is broad. The lymphocyte predominant pleocytosis, normal CSF glucose, and negative CSF cultures raise concern for viral meningoencephalitis. Enteroviruses, herpes simplex virus, and human herpesvirus 6 comprise the most common causes of viral meningoencephalitis in children. Rarer entities include arboviruses, varicella zoster virus, measles, mumps, and others. Rickettsial infections can cause encephalitis but generally present with systemic symptoms such as fever or headache and laboratory abnormalities such as thrombocytopenia or hyponatremia. Neuroinflammatory/autoimmune conditions, including acute disseminated encephalomyelitis, antimyelin oligodendrocyte glycoprotein encephalitis, neuromyelitis optica-spectrum disorders, other autoimmune encephalitides, and certain vasculitides, can present similarly. Acute flaccid myelitis can present with motor deficits but would not cause seizures or affect vision. Metabolic disorders and an accidental ingestion were less likely given normal electrolytes and lactate. Trauma was unlikely with a normal head CT.

A broad diagnostic evaluation was pursued. Repeat CBC showed down-trending leukocytosis of 16,200 cells/μL (16% neutrophils, 33% lymphocytes, and 44% eosinophils; absolute eosinophil count of 6,960). A comprehensive metabolic panel was normal. Repeat LP revealed 50 CSF RBC, 189 WBC (69% eosinophils), protein 38 mg/dL, and glucose 49 mg/dL. Video EEG monitoring demonstrated hemispheric asymmetry with slower frequencies, absent organization, and higher voltages in the left hemisphere. There were rare left temporal sharp waves, but no seizures and no electrographic correlate with staring episodes. MRI of the brain with and without gadolinium demonstrated multifocal supratentorial and infratentorial areas of T2/fluid-attenuated inversion recovery (FLAIR) hyperintensity (Figure 1). Complete spinal MRI was normal. Ophthalmology was consulted and noted evidence of cortical visual impairment but an otherwise normal retinal and ocular examination.

Questions for Consideration:

1. How does this information change the differential diagnosis?
2. What is the significance of the new eosinophilia on LP and CBC?

GO TO SECTION 3

Section 3

The differential diagnosis for serum eosinophilia is broad, including neoplasm, allergy and immunologic disorders, primary eosinophilic disorders, and infections. The neuroimaging and CSF findings in this case are suggestive of a meningoencephalitis. Eosinophilic meningoencephalitis, defined by >10 eosinophils/μL and/or eosinophils accounting for >10% of CSF WBC, is a rare entity accounting for <3% of all CSF samples from patients with pleocytosis.[1] The differential diagnosis for causative organisms is limited, primarily including *Angiostrongylus cantonensis*, *Baylisascaris procyonis*, and *Gnathostoma spinigerum*. Less commonly, other helminthic infections (e.g., toxocariasis and echinococcus), Rickettsial disease, fungal infection (coccidiomycosis and cryptococcosis), and viral infections may also cause eosinophilic meningoencephalitis.

Noninfectious causes of eosinophilic meningoencephalitis include primary hypereosinophilic syndromes, autoimmune disorders (e.g., Churg-Strauss disorder), oncologic processes involving the CNS, drug reactions (e.g., nonsteroidal anti-inflammatory drugs and certain antibiotics), or the presence of a ventriculoperitoneal shunt, none of which were suggested by this child's neuroimaging or clinical course.

"It is important that" automated differentials can misclassify eosinophils as monocytes.[2] This is likely why no eosinophils were seen on initial CBC and CSF studies. Therefore, it is important to obtain a manual differential with Wright-Giemsa stain confirming automated differentials when there is clinical suspicion of an eosinophilic process.

Question for Consideration:

1. What are your next steps in management?

GO TO SECTION 4

Figure 2 Interval Progression of Symmetric, Nonenhancing FLAIR Signal Abnormality (White Arrows) Involving the Bilateral Deep, Periventricular, and Subcortical White Matter (A–C) as Well as Medial Cerebellar Hemispheres (D)
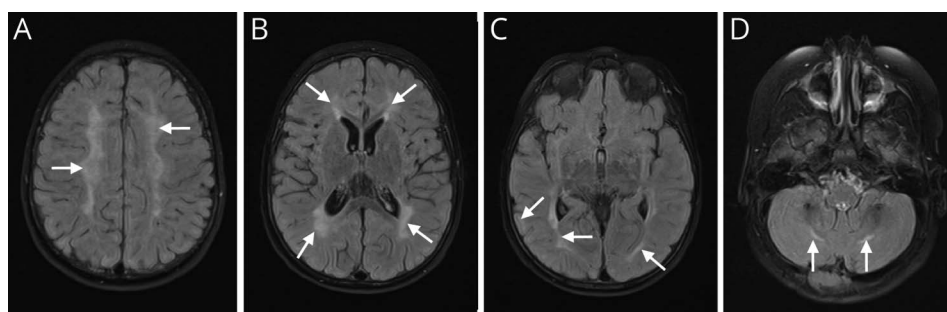
Section 4

Given suspicion for parasitic meningoencephalitis, this child was treated with a 10-day course of corticosteroids (methylprednisolone 20 mg/kg/day for 3 days, followed by prednisolone 2 mg/kg/day for 7 days) and albendazole (40 mg/kg/day divided twice daily) with improvement in coordination and vision. He had no further seizures. His eosinophilia was improved at discharge 5 days later, with an absolute eosinophil count of 1,630 cells/μL. *Baylisascaris procyonis* testing (immunoglobulin G enzyme-linked immunosorbent assay) performed at the Centers for Disease Control and Prevention (CDC) was positive in the serum, but negative in CSF. Other diagnostic testing, including genetic testing for hypereosinophilic syndromes, stool ova and parasites, and CSF metagenomic sequencing, was negative.

At the 4-week follow-up, the child had a subtle residual left-hand preference, but otherwise normal neurologic examination. At the 3-month follow-up, neuro-ophthalmology noted normalized vision for age. At the 4-month follow-up, neurology noted mild delays in ambulation (not walking at age 16 months). A repeat CBC showed rising eosinophilia, with absolute eosinophil count of 1,970 cells/μL. Repeat MRI brain with and without gadolinium demonstrated interval worsening of multifocal areas of symmetric non-enhancing FLAIR signal abnormality throughout the supratentorial white matter (Figure 2). Given concern for disease progression, he was readmitted for evaluation and treatment. LP was notable for CSF WBC 15 (47% eosinophils) and RBC 2,880. He was treated with albendazole for 28 days and methylprednisolone 20 mg/kg/day for 5 days, followed by a 5-week prednisone taper, which he tolerated well. Serial evaluations, most recently 21 months after initial presentation (age 33 months), demonstrated stable neuro-imaging and normalized eosinophil counts. Examination at that time was notable for subtle right hemiparesis, trace right-sided hypertonia with positive right Babinski, and independent ambulation with mildly wide-based gait. Despite subtle gross motor and speech delays, his global development is progressing.

Discussion

Baylisascaris procyonis is an intestinal roundworm that infects raccoons in the United States, although regional prevalence varies. Humans become infected by ingesting eggs, which can survive for years in the soil of raccoon latrines. Infection risk is highest in young children who are prone to pica or geophagia. Clinical symptoms correlate with the volume of embryonated eggs ingested and can present as ocular larval migrans (unilateral retinitis with photophobia and vision loss) and/or neural larval migrans. With neural larval migrans, symptomatic onset occurs within 2–4 weeks of ingestion, starting with fatigue, nausea, fever, and lethargy and then progressing to weakness, incoordination, ataxia, seizures, altered mental status, and later coma.[3,4]

Characteristic neuroimaging findings of CNS *Baylisascaris* infection include T2 prolongation in the deep white matter[5] because larval migration tracks cause necrosis, with secondary inflammation caused by eosinophil degranulation and release of neurotoxic proteins, including interleukin 5.[6] *Baylisascaris procyonis* should be suspected in patients with CSF eosinophilia and white matter lesions on MRI. The diagnosis is confirmed with serum and CSF antibody testing through the CDC. Discordant serum and CSF testing is rare, although 2 other cases have been reported.[7] Morphologic identification through brain biopsy is unlikely to yield a sufficient sample for detection.

Treatment involves antihelminthic agents such as albendazole with concurrent corticosteroids to prevent toxicity secondary to cytokine release from parasite death.[8] The appropriate duration of treatment has not been established. Baylisascariasis is highly morbid. Tissue damage begins before symptomatic onset, so there is a lag in symptom onset from exposure, and diagnosis is often delayed. Of the 31 documented cases with CNS involvement to-date, 5 caused death and nearly all remaining patients had profound neuro-cognitive deficits.[6,8-13] Only 3 prior cases have been described without neurologic devastation: 1 child with mild paraparesis and moderate speech delay[14] and 2 children with full neurologic recovery.[7,15] This case represents a fourth child with remarkable recovery from

what has historically been a devastating disease. Each child was promptly treated with corticosteroids and high-dose albendazole, suggesting that early recognition and treatment are imperative to improving patient outcomes.

Appendix Authors

Name	Location	Contribution
Stephanie Brosius, MD, PhD	Children's Hospital of Philadelphia, Divisions of Oncology and Neurology	Drafting/revision of the manuscript for content, including medical writing content; major role in the acquisition of data; study concept or design; analysis or interpretation of data; and additional contributions: clinical care
William Otto, MD, MSCE	Children's Hospital of Philadelphia, Infectious Disease	Drafting/revision of the manuscript for content, including medical writing content; major role in the acquisition of data; study concept or design; analysis or interpretation of data; and additional contributions: clinical care
Amy Waldman, MD, MSCE	Children's Hospital of Philadelphia, Division of Neurology The Perelman School of Medicine at the University of Pennsylvania, Departments of Pediatrics and Neurology	Revision of the manuscript for content, major role in acquisition of data, additional contributions: clinical care
Michael Russo, MD	Children's Hospital of Philadelphia, Infectious Disease	Drafting/revision of the manuscript for content, including medical writing content; major role in the acquisition of data; study concept or design; analysis or interpretation of data; and additional contributions: clinical care

Appendix (continued)

Name	Location	Contribution
Jennifer McGuire, MD, MSCE	Children's Hospital of Philadelphia, Division of Neurology The Perelman School of Medicine at the University of Pennsylvania, Departments of Pediatrics and Neurology	Drafting/revision of the manuscript for content, including medical writing content; major role in the acquisition of data; study concept or design; analysis or interpretation of data; and additional contributions: clinical care

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