Clinical Reasoning: A 15-month-old boy with progressive lethargy and spasticity

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SECTION 1

A previously healthy and developmentally normal 15-month-old boy presented to the emergency department with 5 days of worsening altered mental status in the setting of an upper respiratory infection. He initially developed cough, rhinorrhea, and irritability without fever, vomiting, or diarrhea. His mental status at home had slowly declined, with increased sleepiness and progressively decreased activity. At the time of presentation, he had stopped playing, walking, sitting, or drinking. On his initial examination, he was breathing comfortably on room air and was afebrile with normal vital signs. He did

not respond to stimuli and had developed intermittent rhythmic shaking of his arms, concerning for seizures. He had no visual tracking and minimal pupil reactivity. He had diffuse hypertonia with bilateral flexion of the upper extremities and extension of the lower extremities without spontaneous movement, minimal withdrawal to noxious stimuli, diffuse hyperreflexia, and several beats of left Achilles tendon clonus.

Question for consideration:

1. What is the differential diagnosis for a toddler with altered mental status?

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SECTION 2

Differential diagnosis for persistent altered mental status in young children is broad and includes sepsis, meningitis, encephalitis, nonconvulsive status epilepticus, postictal encephalopathy, stroke, intracranial mass, head trauma, ingestion, metabolic disorders, hypoglycemia, and electrolyte disturbances.¹ Given the indolent course and previous illness symptoms, the patient's presentation was most concerning for encephalitis.

Empiric antibiotic and antiviral treatment was started, head CT was obtained, and a lumbar puncture was performed. Initial laboratory evaluation was notable for a complete blood count (CBC) showing leukocytosis (leukocytes 15.6 K/mL) with eosinophilia (30.4%) and an elevated erythrocyte sedimentation rate (51 mm/h). Complete metabolic panel, thyroid-stimulating hormone, creatinine kinase, ammonia, and lactate were all within normal limits. CSF studies showed a mild pleocytosis (12 leukocytes) with a monocytic predominance and normal protein and glucose. Urine and blood toxicology screens were negative. Blood and CSF cultures were negative. Respiratory virus PCR was positive for rhinovirus. Continuous EEG showed generalized slowing, but no epileptiform activity. The intermittent arm shaking was captured on EEG and thought to be exaggerated tremulousness secondary to discomfort.

Noncontrast head CT showed a small subdural effusion with mild ventriculomegaly. Brain MRI revealed multifocal cerebral and cerebellar white matter contrast enhancement. Radiographic skeletal survey was negative for fractures, and ophthalmologic examination showed no retinal hemorrhages, though an abnormal retinal sheen of unknown significance was noted.

Initially, the patient's neurologic examination remained relatively unchanged, with persistent significant disability from baseline. Repeat MRI on hospital day 5 showed increased multifocal contrast enhancement in both the supratentorial and infratentorial white matter (figure, A). Given negative CSF culture and viral studies, progression of disease on imaging, lack of clinical improvement on empiric antimicrobial therapy, and persistent peripheral eosinophilia (33.4%) on repeat CBC, lumbar puncture was repeated. Repeat CSF showed 32 leukocytes with an eosinophilic predominance (32%), consistent with eosinophilic meningoencephalitis.

Question for consideration:

1. What is the differential for eosinophilic meningoencephalitis?

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Figure MRI and serial funduscopy examinations

(A) Axial T1 fluid-attenuated inversion recovery MRI with gadolinium shows patchy contrast enhancement and enlarged subdural spaces on hospital day 5. (B) Fundus photograph of the right eye shows atrophic retinal pigment epithelium lesions in random snail track patterns on hospital day 8. (C) Sectoral fundus photograph of the right eye 3 weeks after initial presentation shows atrophic retinal pigment epithelium changes.

SECTION 3

CSF eosinophilia is defined as absolute eosinophil count of $>10/\text{mL}$ CSF or eosinophils $>10\%$ of total CSF leukocyte count.² Causes of CSF eosinophilia in previously healthy individuals include parasitic, fungal, bacterial, and viral infections, rheumatologic disease, neoplasms, idiopathic hypereosinophilic syndrome, allergy, and drug toxicity.² Of etiologies listed, parasitic infections account for a majority of cases of CSF eosinophilia. The 3 most common helminths worldwide that lead to eosinophilic meningoencephalitis are *Angiostrongylus cantonensis*, *Gnathostoma spinigerum*, and *Baylisascaris procyonis*.² *Angiostrongylus* and *Gnathostoma* are both mainly endemic in Asia, although there have been recent reports of cases in the Americas due to ingestion of contaminated shellfish.² *Baylisascaris*, on the other hand, is endemic in North America. This

patient's clinical course fits well with the typical presentation of *Baylisascaris* encephalitis—acute and rapidly progressive lethargy, spasticity, sometimes accompanied by ocular larva migrans, and MRI findings of nonspecific diffuse white matter changes.

A repeat ophthalmologic examination was performed on hospital day 8 to look for signs of ocular larva migrans. The right eye, where previously an abnormal retinal sheen was seen, now revealed random tracks, which were concentrated around the optic nerve (figure, B). The tracks did not follow the blood vessels and there was no vasculitis.

Questions for consideration:

1. How is Baylisascariasis diagnosed?
2. What is the treatment course for *Baylisascaris* meningoencephalitis?

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SECTION 4

Diagnostic testing for *B. procyonis* is only available through the Centers for Disease Control and Prevention (CDC). Both serum and CSF samples, obtained concurrently, should be submitted for testing. Diagnosis is confirmed if there is a positive immunoglobulin G (IgG), as determined by a Western blot assay using antigen rBpRAG1, from the serum or CSF.³ In this patient, testing done by the CDC revealed a positive serum IgG but a negative CSF IgG. Although both serum and CSF antibodies are often positive, there have been multiple similar cases reported where only the serum tested positive.⁴

Due to the relative rarity of this disease, treatment regimens have not been well-studied. In animal models, CNS lesions were reduced after initiation of albendazole, but only if administered within 10 days of infection.² In the majority of reported human cases, once CNS manifestations appear, antihelminthic treatment often had no effect on the disease process. The recommended treatment regimen consists of high-dose albendazole (20–50 mg/kg/d) and steroids given concurrently to mitigate the inflammatory response. There is no clinical guidance for treatment length, but in most reported cases, treatment was continued for at least 1 month.⁴ Albendazole at 25 mg/kg/d and methylprednisolone were started empirically after the discovery of eosinophilia in the CSF, while awaiting testing results from the CDC. After confirmation of the diagnosis, and signs of worsening disease on MRI, the albendazole dose was increased to 50 mg/kg/d. Albendazole was discontinued after 30 days with a steroid taper. Repeat MRI following discontinuation of treatment was stable. The patient required gastrostomy tube placement for feeding prior to discharge home. Three months later, he is visually tracking, is taking some food by mouth, and has minimal vocalizations. He continues to have severe spasticity, despite escalation of treatment, and has developed features of dysautonomia. A source was not ultimately identified as the Department of Health did not find a raccoon latrine near the home and the family dogs tested negative for the parasite.

DISCUSSION *B. procyonis* is a roundworm found in raccoons. An estimated 70%–90% of the US raccoon population is infected with this helminth, with the highest prevalence in the Northeast, Midwest, and West Coast.⁵ Infectious eggs are passed through raccoon feces and can lay dormant in the environment for prolonged periods. Disease in humans and other accidental hosts occur when these eggs are ingested. The majority of patients diagnosed with clinical Baylisascariasis are under 2 years of age because they are more likely to engage in oral exploration of their

environment and therefore more likely to be exposed to *B. procyonis* eggs.⁴ However, the disease has increasingly been diagnosed in older individuals, who fall into 2 subsets: individuals who engage in activities at high risk for contact with raccoon feces, including wildlife management professionals and hunters; and patients with neurocognitive impairment, including those with developmental delay and elderly patients with dementia.² These individuals may display pica or geophagia, increasing the risk of ingestion of *B. procyonis* eggs in the soil. A low infectious dose is needed to cause disease.⁴ Once ingested, the larvae hatch from the eggs and migrate into the tissue of the host, leading to visceral larva migrans, ocular larva migrans, or most commonly, neural larva migrans (NLM). Clinical presentation of NLM and progression of illness is similar in adult and pediatric patients, with acute and rapidly progressing meningoencephalitis, which can be fatal. Rarely, asymptomatic infections and milder disease have been reported. Once neurologic manifestations are observed, prognosis for full neurologic recovery is poor. Treatment with albendazole and steroids has not been shown to improve clinical outcome except when given very early in disease course. Diagnosis is confirmed either through positive *Baylisascaris* antibody from the serum or CSF or by visualization of appropriate-sized larvae in cases of ocular disease. Serial ophthalmologic examinations may reveal the diagnosis earlier than confirmation by serologic testing. Since the helminth does not reproduce outside its definitive host, examination of stool in human cases will not reveal any eggs or larvae.

Recently, Baylisascariasis has become a public health concern due to increasing proximity of raccoon activity to human habitats, even in urban centers. Raccoons prefer to defecate in communal areas, known as latrines, which may be located around the immediate home environment or playgrounds. Due to poor prognosis for the disease and lack of effective therapy, CDC recommends prophylactic administration of 10 days of albendazole for any individual suspected of having contact with raccoon feces, while awaiting investigation of the ingested material.² Once a case of Baylisascariasis is confirmed, careful inspection of the home environment should be conducted to look for signs of raccoon activity and eggs in the environment must be killed with heat, preferably with a propane torch.⁶ Domestic dogs can also serve as a definitive host for *B. procyonis* and shed infectious eggs through their feces, increasing the risk for accidental ingestion for the household members. Baylisascariasis remains an underrecognized and underreported disease. Clinicians should have a high suspicion for Baylisascariasis in any patient who presents with meningoencephalitis with peripheral and CNS eosinophilia.

AUTHOR CONTRIBUTIONS

Rachel Zhang: drafted and revised the manuscript, treated the patient. Julie Ziobro: study concept and design, critical revision of the manuscript for intellectual content, created figure, treated the patient. Jennifer Harmon: drafted and revised the manuscript, treated the patient. Ferdinand Rodriguez Agramonte: provided retinal images and interpretation of retinal findings, edited manuscript for intellectual content. Marijean Miller: provided retinal images and interpretation of retinal findings, edited manuscript for intellectual content. Laura Tochen: critical revision of the manuscript for intellectual content and supervised patient care. Barbara Jantusch: study concept and design, critical revision of the manuscript for intellectual content, supervised patient care. Andrea Hahn: study concept and design, critical revision of the manuscript for intellectual content, diagnostic interpretation and patient care.

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DISCLOSURE

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