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CASES FROM THE PEDIATRIC FELLOWS' DAY WORKSHOP

A Child With Intermittent Headaches and Eosinophilic Meningitis

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CASE PRESENTATION

An 11-year-old previously healthy boy presented to the emergency department in March 2016 after 16 days of intermittent headaches associated with vomiting, 7 days of low-grade intermittent fevers, a wide-based gait, and weight loss. He was treated previously with diphenhydramine, promethazine, and ketorolac for headaches at 2 previous medical visits during this illness. Noncontrast magnetic resonance imaging (MRI) of the brain was performed on day 10 of illness, after his second presentation for medical care; the results were read as normal, and he was discharged home. He ultimately presented to our facility on day 16 of illness for further evaluation of his headaches and vomiting.

The patient was born and raised in Colorado and lived with his parents and 3 siblings in the greater metropolitan Denver area. He had no significant previous medical history, and he had received all recommended immunizations. His overall growth was normal except for a recent 6-lb weight loss, which was attributed to vomiting. No history of a similar or unusual illness in his family or concurrent sick contacts was found. The patient and his family regularly traveled to Mexico to visit family on a farm that had goats and dogs. During these trips, the most recent of which had occurred 7 months before illness onset, he drank only bottled water, the only meat he consumed was chicken, and he did not consume any unpasteurized dairy product.

On presentation, his temperature was 37.4°C, pulse was 61 beats per minute, blood pressure was 140/81 mm Hg, and respiratory rate was 20 breaths per minute, and his peripheral oxygen saturation (Spo_2) was 96% on room air. He was awake, appeared well, and was oriented to time and place. His sensorium and speech were normal, an examination of his cranial nerve function revealed no defect, and we found no nystagmus. He had 2+ upper-extremity reflexes, and his patellar and Achilles reflexes were 3+ on the left and 2+ on the right. Muscular strength was 4/5 (Medical Research Council scale) in the flexors and extensors of his left lower limb and 5/5 in all his other extremities. His abdominal and cremasteric reflexes were normal. His sensations to touch, temperature, and vibration were intact. We found no dysdiadochokinesia, the finger-nose-finger test result was normal, and the Romberg test result was negative; however, he had a wide-spaced gait. The remainder of the examination was unremarkable.

Laboratory evaluation revealed a total peripheral leukocyte count of 14 500/μL with 81% neutrophils, 11% lymphocytes, 5% monocytes, and 2% eosinophils. His hemoglobin concentration was 14 g/dL, hematocrit level was 41%, and platelet count was 348 000/μL. His C-reactive protein level was 1.4 mg/dL, and his erythrocyte sedimentation rate was 14 mm/hour. His cerebrospinal fluid (CSF) opening pressure was 33 mm Hg. CSF cytology revealed 409 leukocytes/mL with 31% lymphocytes, 16% monocytes, and 53% eosinophils, 48 erythrocytes, a CSF glucose concentration of <20 mg/dL, and a CSF protein level of 88.7 mg/dL.

Contrast-enhanced MRI of the brain was performed on day 17 of illness (Figure 1).

DISCUSSION

Differential Diagnosis

Eosinophilic pleocytosis of the CSF is always considered abnormal and warrants urgent diagnostic evaluation for an infectious,

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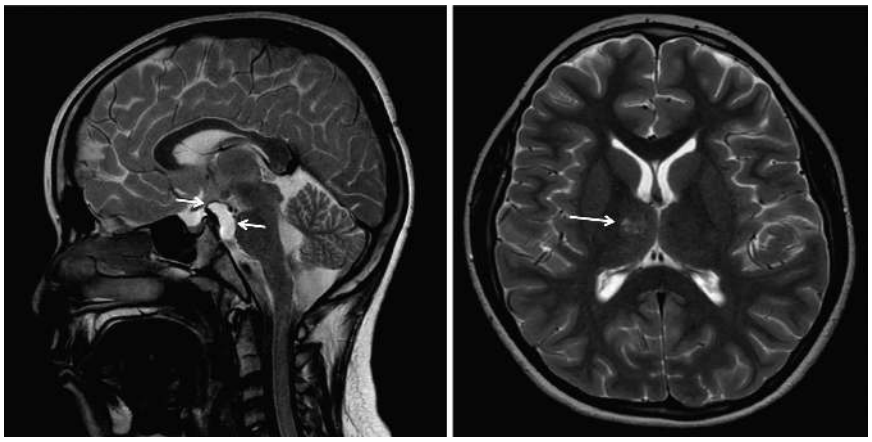

Figure 1. (Left) Sagittal T2-weighted images of the patient's brain reveal a prepontine cystic mass with wall enhancement and ventral mural nodule (arrows). (Right) Axial T2-weighted magnetic resonance image reveals a patchy signal abnormality of the right thalamus (arrow).

oncologic, or medication-related cause. Among the infectious etiologies of eosinophilic meningitis, parasites (predominantly *Angiostrongylus cantonensis* but also *Gnathostoma spinigerum*, *Schistosoma mansoni*, *Taenia solium*, *Baylisascaris procyonis*, *Paragonimus westermani*, *Trichinella spiralis*, and *Toxocara canis*) and fungi (*Cryptococcus neoformans* and *Coccidioides immitis*) are the most common [1]. A complete travel, food, and animal-exposure history is needed to narrow the broad differential diagnosis.

Diagnostic Evaluation

The second contrast-enhanced MRI scan revealed a prepontine cystic mass with a solid mural nodule and a nonenhancing signal abnormality of the right thalamus. The cystic mass with mural nodule, suggestive of a scolex, made cysticercosis the most likely diagnosis based on imaging results. Thalamic signal abnormalities can be seen in those with cryptococcal disease, but it is uncommon in immunocompetent hosts.

Results of a bacterial CSF culture and testing of the CSF for *Cryptococcus* antigen (Mayo Clinic Laboratories, Rochester, Minnesota) were negative. After we obtained consent from his parents, the patient was enrolled in a research study that was using metagenomic next-generation sequencing (mNGS) to identify in CSF the infectious causes of meningitis and/or encephalitis (see Supplementary Data for detailed methods and results of that study). *T solium* was detected in this patient's CSF by mNGS and confirmed by *T solium*-specific polymerase chain reaction testing (see Supplementary Figure 1). Concurrent with the mNGS findings, the results of serum and CSF enzyme-linked immunoassays for immunoglobulin G antibodies to *T solium* were positive with optical densities of 3.55 (reference, ≤0.34 [Quest Diagnostics, Denver, Colorado]) and 30.89 (reference, ≤0.34 [Focus Diagnostics, San Juan Capistrano, California]), respectively.

Treatment and Clinical Course

The patient was treated for 14 days with albendazole and for 10 days with dexamethasone. His headaches and fevers resolved, and he was discharged home on day 7 of hospitalization. At the 2-week follow-up, his gait and strength had returned to normal, although his left lower-extremity reflexes were still brisk (3+). Results of his neurologic examination had normalized completely by the 10-week follow-up visit. Repeat MRI of the brain 1 month after completion of treatment revealed decreased size of the prepontine cyst and improvement of the thalamic lesion.

Teaching Points

Diseases caused by *T solium* include taeniasis (adult tapeworm), associated with the ingestion of raw or undercooked infected pork, and cysticercosis (encysted larvae), associated with the ingestion of food contaminated with egg-containing fecal matter from infected animals or humans [2]. As in this case, the ingestion of pork is not required for the development of cysticercosis. In those with cysticercosis, after intestinal penetration and hematogenous spread, the embryo anchors in terminal vessels of end organs, most notably the brain [3]. The encysted lesions cause little inflammation initially; however, with involution of the cysticercus, inflammation and edema can occur. Calcification ultimately can follow complete involution [4].

Infected people can be asymptomatic and afebrile for years; sometimes calcified cysticerci are found incidentally in neuroimaging studies [3]. However, as seen in this patient, some cysticerci will cause inflammation as they mature and degenerate, which leads to slow-onset headache and/or seizure [2]. In fact, neurocysticercosis is the most common cause of acquired epilepsy in countries in which cysticercosis is endemic [2]. Complications include cranial nerve palsy, ophthalmologic complaints, intracranial hypertension, hydrocephalus, and stroke.

Despite poor reported specificity [3], the diagnosis of neurocysticercosis remains primarily radiographic. Calcifications can be seen with computed tomography scans; however, contrast-enhanced MRI might identify cysts (with laminar scolex), calcifications, or related edema [4], so imaging is typically recommended when neurocysticercosis is suspected. Peripheral eosinophilia is uncommon; however, eosinophilic pleocytosis of the CSF suggests extraparenchymal cysticerci, as seen in this patient and in up to 30% of patients with neurocysticercosis [3]. Antigen testing is unreliable, because circulating serum antigens are transient, and stool antigen testing depends on disease burden [4]. Positive serum antibody results indicate exposure to the organism but do not indicate timing of infection, whereas intrathecal production of antibody detected in CSF confirms neuroinvasive infection [4]. However, false-negative serologic testing results are found in up to 50% of people with just 1 cyst or calcifications alone [4].

In this patient, the eosinophilic CSF pleocytosis and cystic mass with mural nodule made cysticercosis the most likely diagnosis, although it was important to consider cryptococcal infection with the thalamic findings. Treatment was started empirically once cryptococcal testing results were found to be negative, pending confirmatory studies. Specific polymerase chain reaction testing of the CSF might play a role in definitively diagnosing *T solium* [3], but it is directed at only 1 target and might lack sensitivity. Metagenomic sequencing is an emerging diagnostic approach that enables comprehensive identification of potential pathogens in a single assay through the detection of nucleic acid from viruses, bacteria, fungi, and parasites [5]. This case reveals how this unbiased approach might be used to identify or confirm a diagnosis in cases of unexplained meningoencephalitis.

Once a patient is diagnosed with neurocysticercosis, treatment includes albendazole for 14 days as a first-line antiparasitic treatment with concurrent corticosteroids to control the inflammatory reaction from host recognition of the parasite as it dies [2, 4]. In addition, anticonvulsant agents can be used to control or prevent seizures caused by edema from the inflammatory response. Overall, the prognosis of patients with neurocysticercosis depends on many factors, including disease burden, cyst location, and host immune response. Intraparenchymal disease typically is resolved, although some patients experience prolonged headaches and seizures. In patients with extraparenchymal disease, lesions can enlarge and lead to obstructive hydrocephalus, which results in a case fatality rate that is higher than that of parenchymal disease [2]. However, with early recognition and treatment before extraparenchymal cysticerci cause obstruction, as in this case, some patients can be treated successfully without significant morbidity or death.

Supplementary Data

Supplementary materials are available at *Journal of the Pediatric Infectious Diseases Society* online.

Notes

Disclaimer. Contents of this article are the authors' sole responsibility and do not necessarily represent official National Institutes of Health (NIH) views.

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