

Neurocysticercosis: An Unusual Cause of Epileptic Seizures

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Neurocysticercosis (NCC) is the most common parasitic infection of the central nervous system (CNS). It is caused by the parasite tapeworm *Taenia solium*. Clinical manifestations are nonspecific,¹ but NCC is a common cause of seizures in developing countries. Patients with calcified cysts that were previously treated may have seizures that mimic active disease. The diagnosis of central cysticercosis is based primarily on viable cysts with a mural nodule associated with degeneration of cysts and calcifications seen on computed tomography (CT) or magnetic resonance imaging (MRI). Increased travel and immigration from endemic areas has caused a recent increase in the incidence of this parasitic disease in industrialized countries such as the United States. The diagnosis and treatment of this disease are discussed.

CASE PRESENTATION

Patient Presentation and History

A 23-year-old Hispanic man presented to a family practice center with several episodes of tonic-clonic seizures. He had been diagnosed with a tapeworm infection 8 years previously in 1993. His parasitosis was partially treated with antihelminthic agents and phenytoin while he was in Mexico. Therapy with antiparasitics lasted approximately 6 months, at which time he stopped treatment because he was unable to afford the medications. He believed that he had acquired the tapeworm from eating large amounts of poorly cooked pork at a young age.

The patient's wife described his seizures as "total body shakes" associated with tongue biting. He described a preictal aura during which he developed aphasia. Despite anticonvulsant therapy, he continued to have seizures about 5 times per year. On further history, he complained of occasional headaches and neck pain. On one occasion, he discovered a thin worm 2 inches long in his stool. At that time, he developed anal pruritus and hematochezia. The worm was never

identified. In the interim, the patient continued to make frequent trips to Mexico.

Physical and Laboratory Examination

The patient's physical examination was essentially normal. Neurologic examination showed that the cranial nerves were intact, motor strength and sensory perception were intact, deep tendon reflexes were 1+ bilaterally, cerebellar abnormalities were absent, and the Babinski reflex was down-going bilaterally. Subcutaneous nodules were not appreciated.

Laboratory evaluation included complete blood count, basic metabolic panel, vitamin B₁₂, folate, and VDRL/rapid plasma reagin. No abnormalities were detected. The patient's serum phenytoin level was 16.5 µg/mL. An electroencephalogram was normal.

Diagnostic Studies

MRI of the brain with and without contrast was performed. Sagittal T1, axial T1/T2 proton density/fluid-attenuated inversion recovery/diffusion, and contrast-enhanced axial and coronal T1-weighted sequences were performed (**Figure**). A 2 × 1-cm elliptical intra-axial mass was identified in the inferolateral aspect of the left cerebellar hemisphere (below the level of the internal auditory canal). This mass demonstrated a central, slightly hyperintense signal and a peripheral hypodense signal. No surrounding vasogenic edema was present. Further investigation revealed at least 6 other sub-centimeter intra-axial lesions with similar signal characteristics associated with the left temporal lobe, left parietal lobe, and bilateral frontal lobes. These lesions demonstrated cerebrospinal fluid (CSF) signal intensity centrally but no surrounding vasogenic edema.

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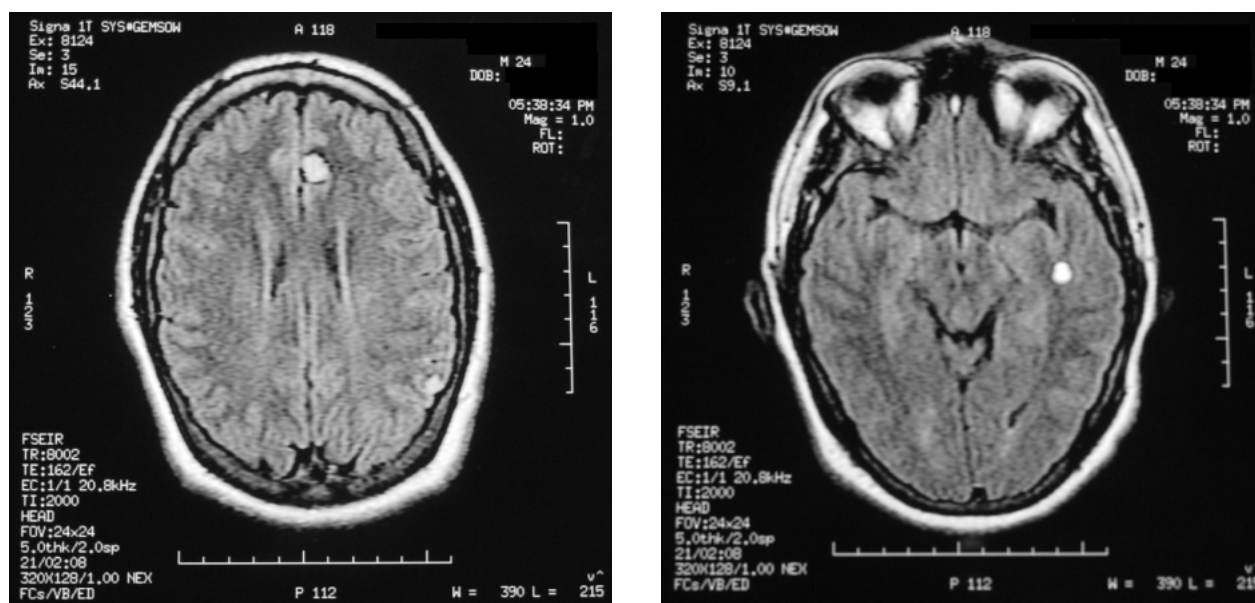


Figure. Fluid attenuated inversion recovery (FLAIR) magnetic resonance images of the case patient's brain. (Left) Well-defined, round/elliptical masses with fluid signal characteristics without mass effect are visible. (Right) An elliptical intra-axial mass with a central, slightly hyperintense signal and a peripheral hypodense signal is visible. No surrounding vasogenic edema is present.

Treatment

The diagnosis at the time was NCC with associated seizure disorder. The discovery of an unidentified worm in the patient's stool was an isolated, incidental occurrence. The patient was started on albendazole 400 mg orally 2 times per day for 30 days. He was given a preparatory regimen of dexamethasone 8 mg orally for 5 days before the use of albendazole.

Outcome

A repeat MRI was done 2 months after starting treatment. This examination displayed minimal difference from the previous study. The patient remained seizure free during this time interval. Because the patient was lost to follow-up, it is unknown whether the MRI findings resolved completely.

DISCUSSION

Epidemiology

NCC, caused by the pork tapeworm *T. solium*, is the most common parasitic infection of the CNS.¹ The natural history of NCC is not well documented. NCC is widely endemic in underdeveloped countries in Central and South America, Asia, and Africa. More than 400,000 people in Latin America^{2,3} and 10% of those with acute neurologic signs in developing countries⁴ have NCC. According to the International League Against Epilepsy, NCC is the most common cause of acquired epilepsy in the developing world, where the

prevalence of seizures is twice that in developed countries.¹ Because of increases in travel and immigration, the disease may appear in nonendemic areas. In the United States, NCC is common among immigrants from endemic areas or adults and children who have contact with these immigrants.

NCC accounts for up to 2% of neurologic and neurosurgical admissions in southern California⁵ and for more than 1000 cases per year in the United States.⁶ Adults in their 30s or 40s are commonly affected. The infection is uncommon in the elderly and in children younger than 2 years because of the long incubation period of *T. solium*. Most children with the disease show a single transitional cyst that resolves over a few months; treatment requires only relief of symptoms and antiseizure medications. A recent epidemiologic study found that household contacts of patients with NCC have a 3-fold higher risk of positive serology than the general population.⁷

Life Cycle, Biology, and Transmission

It takes about 2 months for the larva to develop into a mature adult tapeworm capable of producing eggs.⁸ The adult tapeworm lives in the human small intestine and consists of a scolex and strobila. The strobila consists of proglottids that contain approximately 40,000 eggs.

T. solium can shed up to 300,000 eggs daily into the feces; the eggs are then disseminated into the environment. Free-ranging pigs feed on human feces contaminated with eggs, which develop into cysticerci (cysts

that contain a scolex). Humans acquire intestinal infection by ingestion of undercooked infected pork containing cysticerci, by ingestion of *T. solium* eggs, and by contact with carriers or contaminated food.

Ingested eggs hatch in the stomach and intestine, and the resulting oncospheres circulate in the blood to various tissues. Cysticerci often develop in subcutaneous tissue, skeletal muscle, the brain, the eyes, heart, liver, and lungs. Developing cysticerci cause little host reaction. As cysticerci degenerate, usually after several years, inflammation develops. Ultimately the cysts undergo necrosis and may become calcified. These calcified or dead cysts are antigenic and, when recognized by the host, they may cause an inflammatory reaction.⁹

Egg survival is adversely affected by extremes of temperature and desiccation. Humidity and temperatures between 10°F and room temperature favor egg survival. Wind, water, and birds help in dispersing the eggs.

Classification of Neurocysticercosis

NCC is classified based on the viability and location of the parasite in the CNS of the host. The classification is divided into active (vesicular), transitional (inflammatory, degenerating, or colloidal), granular nodular (healing), and inactive (calcified) stages.¹⁰ Each viability criterion is subdivided into extraparenchymal and parenchymal forms. The viability criterion allows analysis of the parasite's natural history and production of pathophysiologic changes in the host's CNS. Clinical manifestations and therapeutic procedures vary depending on the classification.

Disease Manifestations

The presentation of NCC varies depending on the stage, site, and number of cysts.¹¹ Clinical manifestations develop when an inflammatory response occurs around a cysticercus that is degenerating. What triggers this degeneration is not clear, but the cyst seems to lose its ability to regulate the host immune response. It has been estimated that peak presentation occurs 3 to 5 years after infection, but it can take longer than 30 years. After degenerating, the cysts become calcified and inactive. At this point, they may cease to cause symptoms or may serve as a focus for epileptic activity.

Parenchymal NCC is the most common type of NCC. When a massive number of cysts invades the brain parenchyma, manifestations include seizures (focal or generalized), focal encephalitis, edema, and vasculitis. Any focal neurologic deficits are usually transient, with remissions and relapses. Patients may have headaches and signs of increased intracranial pressure in both the parenchymal and extraparenchymal forms.

Patients with extraparenchymal disease usually present with symptoms of hydrocephalus due to intraventricular cysts. Subarachnoid cysts can cause visual field defects and cranial nerve palsies. Spinal cord cysticercosis is rare.¹² When the spine is affected, the thoracic region is the most common location. Spinal cord cysticercosis can lead to radiculopathy, paresthesias, and sphincter disturbances.

Cysticerci may also develop in the eyes, heart, muscle, or subcutaneous tissue. Ocular cysticercosis is usually asymptomatic. Chorioretinitis, retinal detachment, or vasculitis may result if inflammation occurs around degenerating cysticerci. When the heart is affected, conduction defects and arrhythmias may ensue. Subcutaneous tissue and muscle involvement will result in subcutaneous nodules and myopathy, respectively.

Diagnosis

The differential diagnosis for NCC is vast. The list includes basilar artery thrombosis, stroke, glioblastoma multiforme, medulloblastoma, oligodendroglioma, pituitary tumor, cytomegalovirus, Lyme disease, sarcoidosis, schistosomiasis, toxocariasis, toxoplasmosis, trichinosis, tuberculosis, von Hippel-Lindau disease, and other disorders.

Because the signs and symptoms of NCC are non-specific, diagnosis based on clinical grounds is difficult. Serologic tests have low sensitivity and specificity. Biopsy or autopsy is the only reliable test to confirm pathology¹³; however, neuroimaging studies should be used to evaluate suspected cases of NCC.

Laboratory studies. CSF examination may show inflammatory changes in the case of extraparenchymal cysts. Other CSF findings may include a high protein and leukocyte concentration, low or normal glucose, and an elevated opening pressure. Eosinophils may be the predominate cells found in the CSF.¹⁴ Three consecutive daily stool specimens may be collected for ova and parasite examination. Stool is rarely positive for *T. solium* ova, however, because most patients do not have viable *T. solium* eggs. Electroencephalographic findings do not correlate well with symptoms.

Immunodiagnosis. Immunodiagnostic methods can be used to detect antibodies, which indicate present or past infection. These methods can also detect current infection by the presence of circulating antigens. These methods include complement fixation, indirect hemagglutination, enzyme-linked immunosorbent assay (ELISA), and enzyme-linked immunoelectrotransfer blot (EITB). EITB and ELISA are usually used to diagnose human cysticercosis. The best immunologic diagnostic test is EITB, but ELISA is most widely

used because it is technically simpler. The false-positive and false-negative rates are high, sensitivity is 50%, and specificity is 65% for NCC.¹⁵

Neuroimaging. CT and MRI are the main tools for the diagnosis of NCC, and either can be considered the gold standard. Both CT and MRI can identify the 4 stages of NCC. The most common image is a viable cystic lesion with a mural nodule associated with transitional or degenerative cysts and calcifications. MRI is better for showing intraventricular or subarachnoid cysts, whereas CT is better for detecting calcifications of inactive lesions and edema around cysts.

Treatment

NCC should be treated based on its pathogenesis and natural history in each individual. Because various stages of the parasite may be present, it is important to stage this infection for accurate prognosis and treatment. Therapeutic options include symptomatic treatment with antiepileptic agents, specific antihelminthic therapy with albendazole or praziquantel together with corticosteroids, or surgery.

Albendazole is the preferred antihelminthic therapy because it can destroy intraventricular cysts as early as 3 weeks, with cysts totally disappearing within 3 to 6 months. Recent studies have demonstrated that 7 days of treatment with albendazole is as effective as 14 days.^{16,17} Praziquantel is considered a second-line medication. Serum levels of praziquantel are decreased when used together with combination with steroids, phenytoin, or phenobarbital. The dosage and duration of antihelminthic therapy are presented in the **Table**.

Treatment may cause inflammation around the cysticerci; therefore, steroids (dexamethasone 4–16 mg/d or prednisone 60–100 mg/d) are usually given. Corticosteroids are usually administered 1 to 2 days before and during treatment with albendazole or praziquantel to minimize these inflammatory reactions.

Recommendations for treatment depend on the number of cysts. Antiparasitic treatment is indicated for 5 to 50 cysts, and symptomatic or antiparasitic medication is best for fewer than 5 cysts. When more than 50 cysts or cysticercal encephalitis is present, neurologic deterioration may occur due to inflammation. The benefits of antiparasitic treatment in this setting is questionable; these patients therefore should be managed with steroids alone or steroids with mannitol. Antihelminthic treatment can be started when the edema improves.

Data on the clinical benefits of treatment with antiparasitic agents are conflicting.¹⁸ Pertinent treatment

Table. Recommended Dosage and Duration of Antihelminthic Therapy

Medication	Dosage	Duration, days
Albendazole	15 mg/kg daily divided tid	8–28
Praziquantel	50 mg/kg daily divided tid	15

tid = 3 times daily.

issues include acute inflammation due to death of the cyst, natural resolution of degenerated lesions within 2 years, and scarring secondary to inflammation. A recent double-blind, placebo-controlled study found that generalized seizures were significantly reduced after treatment with albendazole versus placebo.² The rate of partial seizures also decreased, although this reduction was not statistically significant. This study also showed that albendazole resulted in faster resolution of cerebral cysts compared with placebo.²

CT should be repeated 3 to 6 months after therapy to determine whether any of the cysts are still viable. Active parenchymal cysts may become inflammatory or they may calcify into inactive forms within 1 to 6 months.¹⁹ Inflammatory cysts cause symptoms and require antiepileptic agents. Because inflammatory cysts coexist with active cysts, which may not be found by neuroimaging, antihelminthic medications should be considered to eradicate the parasite in active cysts. Calcified cysts may serve as seizure foci and will not disappear with antiparasitic treatment; therefore, they should not be treated with these medications.

When patients exhibit significant disability from neurologic symptoms, neurosurgical intervention should be considered. Medical management should be tried first, but if antiparasitic therapy fails, surgery may prove useful for intraventricular cysts. Ventriculo-peritoneal shunts are required in patients with hydrocephalus.

Prognosis

Parenchymal forms of NCC have a good prognosis in terms of remission of clinical signs.²⁰ The prognosis for extraparenchymal forms is unfavorable, especially in patients with hydrocephalus due to arachnoiditis.²⁰

Prevention

Prevention should be a primary public health focus worldwide. Prevention can be achieved through sanitation, improvement of public health systems, enforcement of meat inspections, and adequate freezing or cooking of pork.

Vaccination is currently not immunologically or logistically feasible. Human protective or therapeutic vaccinations to prevent cysticercosis are not widely considered appropriate in endemic regions because little is known about the immunology of human cysticercosis. Vaccinating pigs would be a good way to break the parasite's life cycle.¹³ Field trials have shown usefulness of vaccines derived from cysticercal extracts.

CONCLUSION

NCC is a parasitic infection of growing importance in the United States. Epidemiologic information of patients, such as birthplace and travel habits, should be considered. Individuals who have never traveled to endemic countries may also acquire NCC from tapeworm carriers and from infected individuals born in nonendemic countries. Therefore, primary care physicians should consider NCC when formulating a differential diagnosis for disease. **HP**

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