Neurocysticercosis

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Neurocysticercosis is a leading cause of seizures and epilepsy in the developing world and is an increasingly important health issue in the United States. Recent results from the Cysticercosis Working Group in Peru provide new evidence supporting the use of antiparasitic agents in highly selected patients with active cysts and seizures.

Introduction

Cysticercosis is a parasitic infection that results from ingestion of eggs from the adult tapeworm, *Taenia solium* (*T. solium*) (1,2). When cysticercosis involves the central nervous system, it is called neurocysticercosis. Neurocysticercosis is the most common parasitic infection of the brain and a leading cause of epilepsy in the developing world, especially Latin America, India, Africa, and China (1–12).

Once largely the domain of the developing countries, neurocysticercosis is currently a growing public health problem in the United States (13,14). Because millions of people have immigrated to the United States from Latin America in recent years, neurocysticercosis has become an increasingly important cause of seizures in the United States (14). For example, between 1994 and 1998, an average of 120 patients with cysticercosis were admitted to Los Angeles County/USC Medical Center per year (15,16), which was a substantial increase from 1983, when 80 cases were identified in all four Los Angeles County hospitals together (13). Cysticercosis now accounts for up to 10% of emergency room visits for seizures in the southwestern United States (14).

Natural History

Neurocysticercosis is acquired through consumption of food contaminated with feces of a *T. solium* tapeworm carrier (i.e., through fecal–oral contract) (4,5,12). The life cycle of *T. solium* is shown in Fig. 1. Eggs of the tapeworm are shed in stool and contaminate food through poor hygiene. When these eggs are ingested and exposed to gastric acid in the human stomach, they lose their protective capsule and turn into larval cysts, called oncospheres. Oncospheres cross the gastrointestinal tract and migrate via the vascular system to the brain, muscle, eyes, and other structures. Once in the brain, the larval cysts (cysticerci) initially generate a minimal immune response and may remain in the brain as viable cysts for years.

Figure 2 shows the four stages of cysts within the parenchyma of the brain: vesicular, colloidal, nodular/granular, and calcified granulomas. The viable larval cyst is known as a vesicular cyst (Fig. 2A) and has minimal enhancement, which is due to little or no host immune response. At this stage, the scolex usually is identified as an eccentric nodule within the cyst. As the cyst degenerates, fluid from the larval cyst leaks into the parenchyma, generating a strong immune response, characterized by enhancement on contrast computed tomography (CT) and magnetic resonance imaging (MRI). An enhancing cyst, without a well-defined scolex, is termed a colloidal cyst (Fig. 2B). As the cyst further deteriorates, it forms a nodule, which continues to demonstrate contrast enhancement (Fig. 2C). Finally the degenerating cyst forms a calcified granuloma, which is recognized as nonenhancing punctuate calcifications on CT (Fig. 2D). Cysts that lodge in the cisterns or ventricles of the brain may cause hydrocephalus and frequently do not have a scolex (e.g., racemic cysts).

Presentation

Neurocysticercosis typically is first seen either with seizures (70% to 90% of acutely symptomatic patients) or headache (4,5,7,11,12). Headache usually indicates the presence of hydrocephalus, meningitis, or increased intracranial pressure. When hydrocephalus is present, the use of antiparasitic drugs is relatively contraindicated, unless a shunt is placed before administration. The mortality rate of patients with hydrocephalus or increased intracranial pressure is higher than the mortality rate of patients with seizures (16).

Epileptogenesis in Neurocysticercosis

Generally, patients with neurocysticercosis have partial-onset seizures with or without secondary generalization (6). At the time of a first seizure, most patients have an active cyst—either a vesicular cyst (Fig. 2A) or a colloidal cyst (Fig. 2B) (11).

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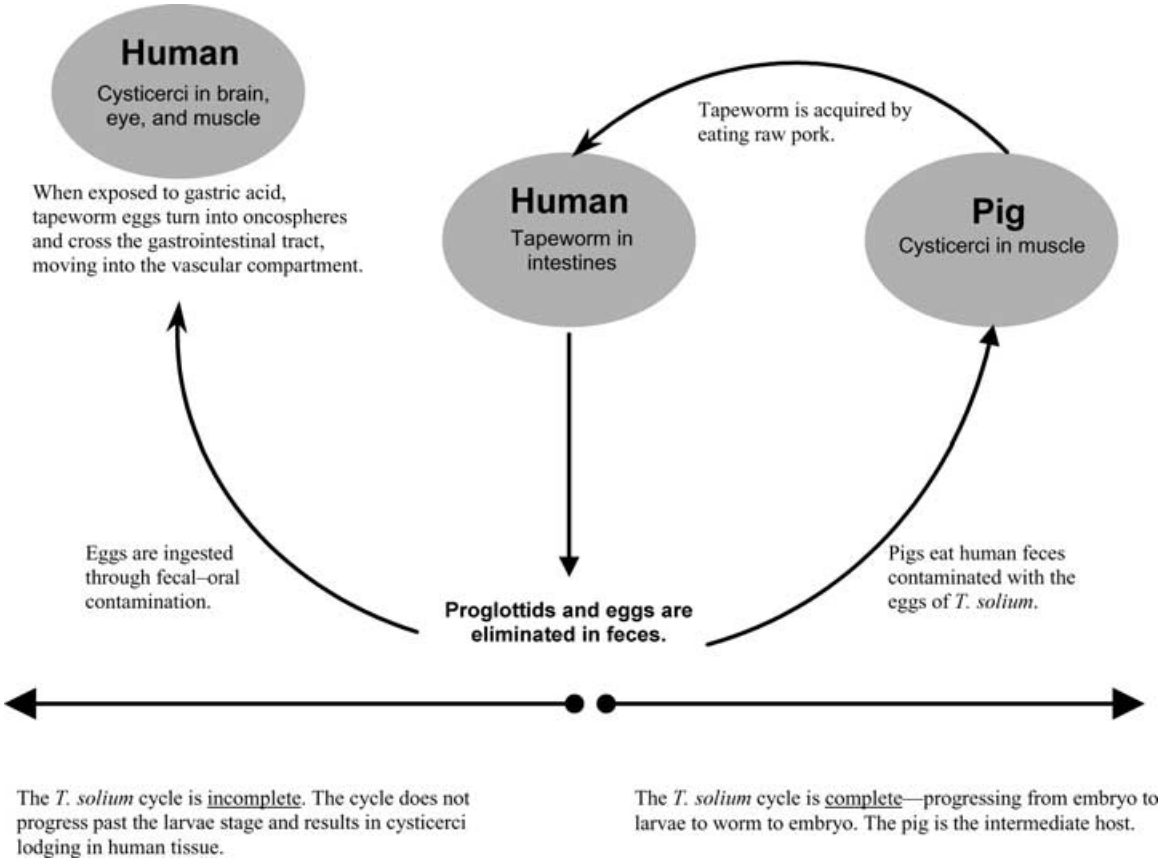

FIGURE 1 Life cycle of *Taenia solium*.

New-onset seizures are commonly associated with active cysts rather than calcified granulomas (11,19). Chronic epilepsy is usually associated with calcified granulomas (6,11,17–19). Cysts that are active and undergoing degeneration (colloidal cysts) are the most epileptogenic. Cysts degenerate fastest within 6 to 12 months after initial presentation (19). Seizure-recurrence rates also increase during the same period, because of the conversion from vesicular cysts to colloidal cysts (19). Animal data support the concept that active or degenerating cysts (vesicular or colloidal) are the most epileptogenic (20). Products from acute cysts injected into animal brains are significantly more epileptogenic than are products from chronic granulomas (20).

Epileptogenesis in patients with neurocysticercosis can be attributed to several factors: inflammation, gliosis, genetics, and predilection for the cysts to travel to the frontal and temporal lobes (17,18,20–23). The host response to degenerating cysts plays an important role in the associated epileptogenesis (22). In children and young women, a profound host reaction develops to parasitic infection of the brain, whereas adults have a more variable response. Within-subject responses also vary. For example, in the same patient, intense inflammation may surround one cyst, whereas an adjacent cyst may show no inflammation (17,19).

Treatment

Albendazole and praziquantel are the principal antiparasitic drugs used to treat neurocysticercosis (1,2,12,19,22–27). Whether and when antiparasitic drugs should be administered is controversial. Data from open-label trials suggest that praziquantel and albendazole reduce the number of cysts and frequency of seizures (23–25,30). In a seminal study, Vasquez and Sotelo (30) found that seizure-free rates at 3 years, for those offered antiparasitic therapy, were significantly higher than those of a nonrandomized control group (94% seizure free). This finding is supported by data from Del Brutto et al. (11), who found that 83% of those individuals who received antiparasitic treatment became seizure free, compared with only 26% of those patients who did not receive treatment.

Some authors suggest that antiparasitic treatment might be counterproductive and expose patients to increased risk (12,27). The risks of antiparasitic therapy include gastrointestinal side

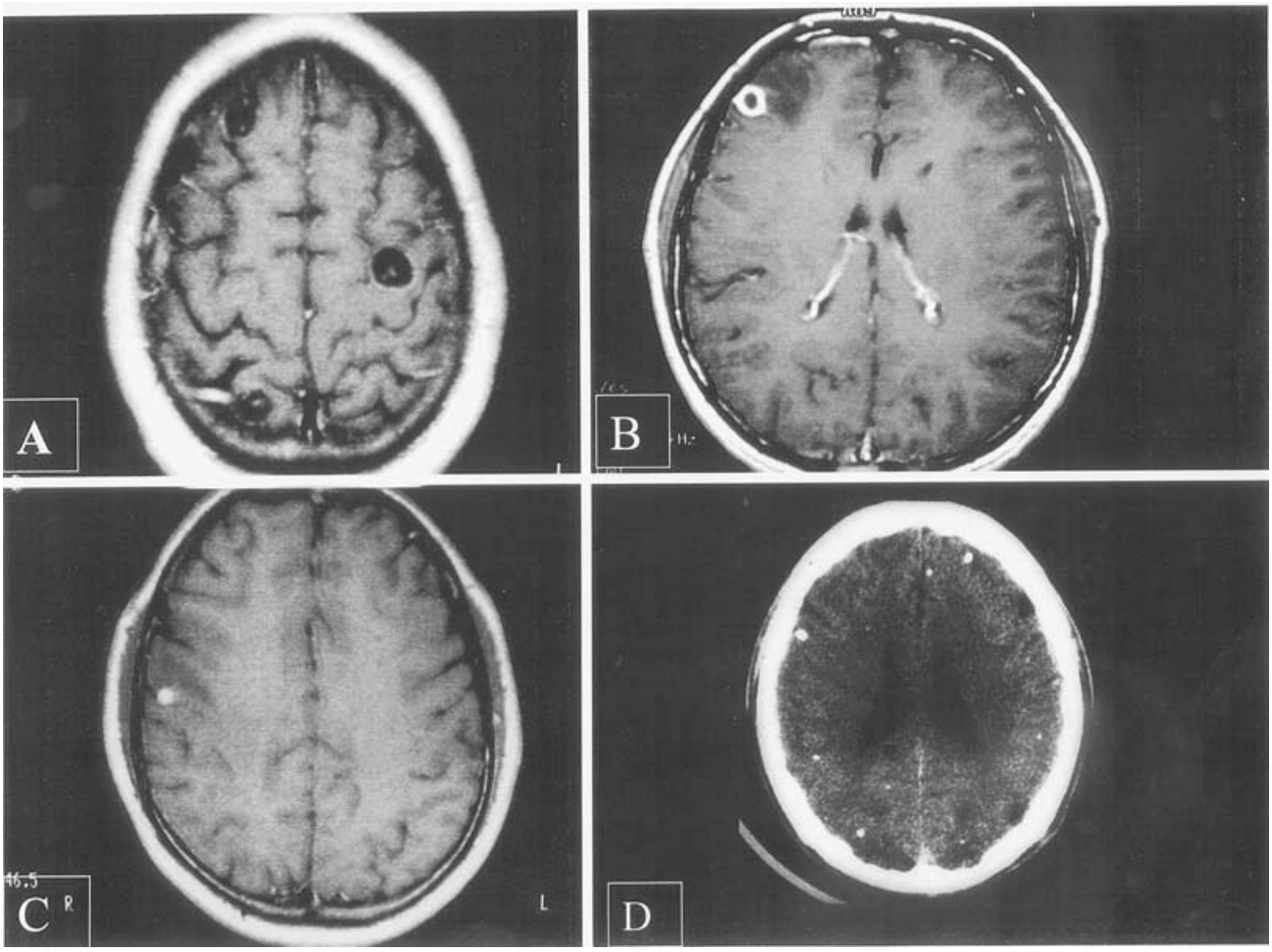

FIGURE 2 Brain imaging demonstrating the four stages of parenchymal neurocysticercosis. **A**: Magnetic resonance imaging (MRI) of a vesicular cyst. Note the well-defined scolex, minimal contrast enhancement, and mass effect. **B**: MRI of a colloidal cyst. Note ring enhancement, loss of the scolex, and perilesional edema. **C**: MRI of the nodular/granular stage. Note nodule with diffuse enhancement and no cystic component. **D**: Noncontrast computed tomography showing multiple punctuate calcifications.

effects, acute seizures, increased intracranial pressure, and rarely, death (1,12,16,26). Side effects, although usually mild, include nausea, headache, seizures, and occasionally, cerebral edema (26,27). Deaths associated with antiparasitic treatment are rare (1% to 4%) and occur primarily in patients with hydrocephalus, increased intracranial pressure, and heavy cyst burden (i.e., more than 20 cysts) (16). In the first randomized comparison of albendazole, praziquantel, and steroids for the treatment of active cysts, Carpio (27) found no significant difference in seizure-free rates among the three treatment groups.

Recently, however, the Cysticercosis Working Group in Peru compared the efficacy and safety of albendazole (400 mg twice a day) with placebo for the treatment of active cysts associated with seizures (31). As in the study of Carpio et al., total seizure-recurrence rates at long-term follow-up were no different for the active and control groups (27,31). However, patients randomized to albendazole experienced a significant (67%) reduction in generalized tonic–clonic seizures compared with the control group (31). Safety was excellent, and no deaths were reported. The low death rate may have been due to the relatively small size of the study ($n = 120$; 60 in each treatment group) and the exclusion of patients with increased intracranial pressure. This study is a major advance, for it is the first randomized, placebo-controlled clinical trial to demonstrate that albendazole substantially reduces generalized tonic–clonic seizure recurrence (31).

Prognosis

In adults and children first seen with new-onset seizures and active cysts, seizure recurrence rates at 4 years are as high as 49% (19). After a second seizure, the estimated risk of recurrence is 68% at 6 years (19). Prognosis is best for those patients in whom imaging studies normalize. The recurrence rate for

those patients with persisting, active cysts (61%) is more than double the rate of patients with normal imaging (22%) (19). Seizure recurrence is reduced in patients who initially have calcifications rather than active cysts (11,17,18). Del Brutto et al. (11) found that patients first seen with new-onset seizures and calcifications fared better than those with active cysts: 100% with calcifications were seizure free at 2 years, compared with 83% with active cysts. Durón et al. similarly found that among 25 patients initially seen with calcifications, seizures remitted in 62.8% (17).

Conclusion

Neurocysticercosis is a leading cause of epilepsy in the developing world and is increasingly prevalent in the United States. New data from the Cysticercosis Working Group indicate that treatment with albendazole significantly improves the prognosis for the recurrence of generalized tonic–clonic seizures in highly selected patients. Results of this trial should not be applied to high-risk patients, such as those with heavy cyst burden or increased intracranial pressure. Better understanding of the mechanisms of neurocysticercosis and the life cycle of *T. solium* is needed to develop appropriate intervention and prevention programs. Global strategies for prevention and control should be developed and enforced with the aid of international health organizations, including the World Health Organization.

References

1. Garcia HH, Gonzales AE, Evans CAW, Gilman RH. *Taenia solium* cysticercosis. Lancet 2003;362:547–556.
2. Sotelo J, Del Brutto OH. Review of neurocysticercosis. Neurosurg Focus 2002;12:1–6 http://www.neurosurgery.org/focus/jun02/12-6-nsf-toc.html.
3. Bittencourt P, Adamolekum B, Bharucha N, et al. Epilepsy in the tropics, II: Clinical presentations, pathophysiology, immunologic diagnosis, economics and therapy. Epilepsia 1996;37:1121–1127.
4. Roman G, Sotelo J, Del Brutto O, Flisser A, Dumas M, Wadia N, et al. A proposal to declare neurocysticercosis an international reportable disease. Bull WHO 2000;78:399–406.
5. Medina MT, DeGiorgio C. Introduction to neurocysticercosis: A worldwide epidemic. Neurosurg Focus 2002;12:6. http://www.neurosurgery.org/focus/jun02/12-6-nsf-toc.html.
6. Medina MT, Rosas E, Rubio-Donnadieu F, Sotelo J. Neurocysticercosis as the main cause of late-onset epilepsy in Mexico. Arch Intern Med 1990;150:325–327.
7. Sanchez AL, Lindback, Schantz PM, Sone M, Sakai H, Medina MT, Lunstrom I. A population-based, case-control study of *Taenia solium* taeniosis and cysticercosis. Ann Trop Med Parasitol 1999;93:247–258.
8. Bharucha NE. Epidemiology of epilepsy in India. Epilepsia 2003;44(suppl 1):9–11.
9. Rajshekhar V, Joshi DD, Doanh NQ, van De N, Xiaonong Z. *Taenia solium* taeniosis/cysticercosis in Asia: Epidemiology, impact and issues. Acta Trop 2003;87:53–60.
10. Jallon P. ILAE Workshop report: Epilepsy in developing countries. Epilepsia 1997;38:1143–1151.
11. Del Brutto OH, Santibanez R, Noboa CA, Aguirre R, Diaz E, Alarcon TA. Epilepsy due to neurocysticercosis: Analysis of 203 patients. Neurology 1992;42:389–392.
12. Carpio A. Neurocysticercosis: An update. Lancet Infect Dis 2002;2:751–762.
13. Richards FO Jr, Schantz PM, Ruiz-Tiben E, Sorvillo FJ. Cysticercosis in Los Angeles County. JAMA 1985;254:3444–3448.
14. Ong S, Talan D, Moran G, Mower W, Newdow M, Tsang VCT, Pinner RW, the Emergencyt IDNET Study Group. Neurocysticercosis in radiographically imaged seizure patients in U.S. emergency departments. Emerg Infect Dis 2002;8:608–613.
15. Ko D. Seizures in neurocysticercosis at LAC+USC Medical Center. Epilepsia 2003;44(suppl 9):15.
16. DeGiorgio CM, Houston I, Oviedo S, Sorvillo F. Death associated with cysticercosis: Report of three cases and review of the literature. Neurosurg Focus 2002;12:1–4. http://www.neurosurgery.org/focus/jun02/12-6-nsf-toc.html.
17. Durón R, Medina MT, Osorio J, et al. Prognosis of the epilepsy due to neurocysticercosis: A five-year follow-up from the Salamá epilepsy study in Honduras. Epilepsia 2003;44(suppl.8):38.
18. Sanchez AL, Ljunstrom I, Medina MT. Diagnosis of human neurocysticercosis in endemic countries: A clinical study in Honduras. Parasitol Int 1999;48:81–89.
19. Carpio A, Hauser A. Prognosis for seizure recurrence in patients with newly diagnosed neurocysticercosis. Neurology 2002;59:1730–1734.
20. Stringer JL, Marks LM, White AC Jr, Robinson P. Epileptogenic activity of granulomas associated with murine cysticercosis. Exp Neurol 2003;183:532–536.
21. Clark S, Silson W. Mechanisms of epileptogenesis. In: Delgado-Escueta, et al., eds. Jasper's basic mechanisms of the epilepsies, 3rd ed.: Advances in neurology. Philadelphia: Lippincott Williams & Wilkins, 1999:79, 607–630.
22. Sotelo J. Neurocysticercosis: Clinical, prognostic and therapeutic aspects. In: Rose C, ed. Recent advances in tropical neurology. Amsterdam: Elsevier Science, 1995:87–97.
23. Sotelo J, Escobedo F, Rodríguez, et al. Therapy of parenchymal brain cysticercosis with praziquantel. N Engl J Med 1984;310:1001–1007.
24. Medina MT, Genton P, Montoya MC, et al. Effect of the anticysticercal treatment on the prognosis of epilepsy in neurocysticercosis: A pilot trial. Epilepsia 1993;34:1024–1027.
25. Sotelo J, Del Brutto OH, Penagos P, et al. Comparison of therapeutic regimen of anticysticercal drugs for parenchymal brain cysticercosis. J Neurol 1990;237:69–72.
26. Salinas R, Counsell C, Prasad K, Gelband H, Garner P. Treating neurocysticercosis medically: A systematic review of randomized, controlled trials. Trop Med Int Health 1999;4:713–718.
27. Carpio A, Santillan F, Leon P, Flores C, Hauser WA. Arch Intern Med 1995;155:1982–1988.
28. Del Brutto OH, Rajshekhar V, White AC, et al. Proposed diagnostic criteria for neurocysticercosis. Neurology 2001;57:177–183.

29. Kramer LD, Locke GE, Byrd S, Daryabagi J. Cerebral cysticercosis: Documentation of natural history with CT. Radiology 1989;171:459–462.
30. Vasquez N, Sotelo J. The course of seizures after treatment for cerebral cysticercosis. N Engl J Med 1992;327:696–701.
31. Garcia HH, Pretell J, Gilman R, Martinez SM, Moulton LH, del Brutto O, Herrera G, Evans CA, Gonzalez AE and the Cysticercosis Working Group in Peru. A trial of antiparasitic treatment to reduce the rate of seizures due to cerebral Cysticercosis. N Engl J Med 2004;350:259–258.