Neurocysticercosis

Neurocisticercose

Osvaldo M. Takayanagui

ABSTRACT
Cysticercosis is one of the most common parasitic diseases of the nervous system in humans, and constitutes a major public health problem for most of the developing world. The clinical manifestations of neurocysticercosis (NCC) largely depend on the host immune response against the parasite. NCC diagnosis is based upon neuroimaging studies (computerized tomography, magnetic resonance imaging) and antibody/antigen detection in the serum and the cerebrospinal fluid. Anticysticercal therapy has been marked by an intense controversy. Randomized controlled trials evaluating the clinical benefit of treatment have yield conflicting data with some studies indicating a benefit and others failing to show a difference. Prevention strategies must rely on multiple approaches, tailoring each to the special features of the particular endemic area.

Keywords: cysticercosis, Taenia solium, epilepsy, albendazole, praziquantel.

RESUMO
A cisticercose é uma das doenças parasitárias mais frequentes do sistema nervoso humano e constitui grave problema de saúde pública na maioria dos países em desenvolvimento. As manifestações clínicas da neurocisticercose (NCC) estão na dependência do número, tipo, localização e estágio de desenvolvimento dos cisticercos, assim como da resposta imunológica do hospedeiro contra o parasita. O diagnóstico da NCC é baseado nos exames de neuroimagem (tomografia computadorizada, ressonância magnética) e na detecção de antígenos/anticorpos no soro e no líquido cefalorraquiano. O tratamento antiparasitário tem sido marcado por uma intensa controvérsia. Os ensaios controlados e randomizados avaliando os benefícios clínicos da terapêutica têm revelado dados conflitantes em que alguns estudos indicam um benefício e outros não. As estratégias de prevenção devem ser fundamentadas na adoção simultânea de múltiplas medidas, adaptadas às características específicas de uma determinada região endémica.

Palavras-Chave: cisticercose, Taenia solium, epilepsia, albendazol, praziquantel.

Cysticercosis, an infection caused by the encysted larval stage of the tapeworm Taenia solium, is one of the most common parasitic diseases of the nervous system in humans, and constitutes a major public health problem for most of the developing world.

Clinical features
The clinical manifestations of neurocysticercosis (NCC) largely depend on the number, type, size, localization, and stage of development of cysticerci, as well as on the host immune response against the parasite. There are no pathognomonic features or a typical NCC syndrome.

Whenever NCC is intraparenchymal it is usually associated with a good prognosis. Frequently, patients with few intraparenchymal cysts remain asymptomatic, although some patients develop seizures. On the other hand, in patients with massive cerebral infection, uncontrolled seizures and cognitive deficit may develop.

Seizures are the most common manifestations of NCC (70–90%) of patients, followed by headache (38%), focal deficits (16%) and signs of intracranial hypertension (ICH) (12%). Other manifestations occur in less than 10% of symptomatic patients.

While many patients present with single or group of seizures at various stages of NCC, not all patients develop recurrent seizures or epilepsy. A series including mostly patients with mild forms of infection showed that about 50% of patients with NCC presenting a seizure have further seizures.

When cysticerci lodge within the ventricular system a life-threatening acute intracranial hypertension secondary to hydrocephalus may develop. It is directly related to obstruction of the flow of CSF by the cyst or by inflammatory reaction of the ependyma. Although the cysts may be found anywhere within the ventricular system, the fourth ventricle is most commonly involved.
Cysts in the subarachnoid space may invade the Sylvian fissure and grow to large sizes, reaching several centimeters in diameter (giant cysts), causing intracranial hypertension with hemiparesis, partial seizures or other focal neurological signs. Subarachnoid cysts may also invade the basal cisterns; initially the growing membranes resemble a bunch of grapes, hence this form of disease is called “racemose” cysticercosis. It is associated with an intense inflammatory reaction, fibrosis and progressive thickening of the leptomeninges at the base of the brain. In approximately 50-60% of the cases, there is an obstruction of the CSF circulation, resulting in hydrocephalus and progressive intracranial hypertension and mortality over 20% of cases. When hydrocephalus secondary to cysticercotic meningitis is present, mortality is high (50%), and most patients die within 2 years after CSF shunting. Therefore, ventricular and basal cisternal locations are considered to be malignant forms of neurocysticercosis.

Diagnosis

The diagnosis of NCC is based upon neuroimaging studies and antibody/antigen detection in the serum and the cerebrospinal fluid (CSF).

Neuroimaging is essential to the diagnosis of NCC. Early in the infection, a viable cyst appears as a spherical hypodense lesion on computerized tomography (CT) and as a CSF-like signal on magnetic resonance imaging (MRI). Both CT and MRI are able to show the invaginated scolex. In the degenerative phase, the cyst shows a ring-like or a nodular contrast enhancement, with or without perilesional edema. A final stage is observed when the cyst dies and a process of mineralization and resorption takes place, resulting in a calcified nodule.

Since the cyst membrane is thin and the fluid is isodense within the CSF, noninflamed extraparenchymal (ventricular or subarachnoid) cysticerci are usually not visible on CT and may only reveal subtle, indirect findings on MRI scans.

Analysis of CSF samples is an important parameter for the assessment and follow-up of patients with a suspicion of NCC. The most frequent CSF alterations are mononuclear pleocytosis and the presence of eosinophils and specific antibodies detected by enzyme-linked immunosorbent assay (ELISA) or enzyme-linked immunoelectrotransfer blot assay (EITB).

Because clinical manifestations are pleomorphic, most neuroimaging findings are not pathognomonic, and several immunological tests show low levels of sensitivity and specificity. Del Brutto et al. have proposed a diagnostic criterion for NCC based on a consensus meeting on cysticercosis.

Treatment of NCC

The treatment modalities available to patients with NCC include surgery, symptomatic therapy and antiparasitic drugs.

The symptomatic therapy is probably more important in NCC than in any other infectious disease. Most patients with NCC present seizures and the administration of standard doses of a single-first-line antiepileptic drug such as phenytoin or carbamazepine usually results in adequate seizure control.

The optimum length of antiepileptic drug therapy has not yet been determined, but it has been suggested that it should be continued until serial neuroimaging studies show resolution of acute lesions.

Since inflammation is the conspicuous accompaniment in most forms of NCC, corticosteroids represent the primary form for attenuating the inflammatory reaction that may cause severe recurrent seizures, focal neurological symptoms and intracranial hypertension syndrome. Additionally, corticosteroids are fundamental for patients with cysticercal encephalitis, arachnoiditis and angiitis. Only scarce controlled data exist to determine when and what type of corticosteroids and the treatment regime to use. Symptomatic treatment includes also the placement of ventricular shunts for hydrocephalus associated with intracranial hypertension syndrome.

Anticysticercal drugs

Therapy for NCC, formerly restricted to palliative measures, has advanced with the advent of two drugs considered to be effective: praziquantel (PZQ) and albendazole (ALB).

The goal of anticysticercal therapy is the simultaneous destruction of multiple cysts then controlling the resulting inflammatory reaction with steroids. This strategy of preventing prolongation of brain inflammation due to degeneration of multiple cysts at different times would allow better clinical evolution than the natural progression of NCC.

Most comparative investigations have shown that ALB is more effective than PZQ in reducing the number of cysts and in inducing overall clinical improvement, with a lower frequency of adverse reactions. However, most of these trials have been uncontrolled, observational imaging studies and none of them were designed to evaluate seizure control. The meta-analyses of comparative trials suggested that ALB is more effective than PZQ regarding clinically important outcomes in patients with NCC.

Controversies over anticysticercal therapy

Anticysticercal therapy has been marked by an intense controversy. The descriptions of spontaneous resolution of parenchymal cysticercosis with benign evolution, risks of complications and reports of no long-term benefits have reinforced the debate over the usefulness and safety of anticysticercal therapy.

Most available data describing the effectiveness of anticysticercal treatment are from uncontrolled studies with a significant selection bias. Many studies have documented that antiparasitic therapy results in death and resolution...
of viable cysts, but the clinical benefit of this treatment has been questioned. Randomized controlled trials evaluating the clinical benefit of treatment have yielded conflicting data with some studies indicating a benefit and others failing to show a difference. A systematic review by the Cochrane Collaboration concluded that although evidence from trials of adults with viable cysts suggests ALB may reduce the number of lesions, no difference was detected for recurrence of seizures.

**Control and preventive measures**

By the first part of 20th Century, *Taenia solium* infections had been almost eradicated in Europe. This process took place several decades and required many changes in economic, educational and sanitary standards, and improvement in the effectiveness of medical and veterinary services, especially meat inspection. These are not likely to be duplicated soon in many parts of the developing world. Therefore, the realistic aim of control is to reduce the incidence and prevalence of *T. solium* infections in humans and pigs to the level that human neurocysticercosis does not constitute a major public health and economic problem in a given endemic area.

Potential strategies for the control of *Taenia solium* infections have been updated recently. Of the six proposed approaches, three (based on medical and veterinary interventions) have the potential to meet short-term control goals. These are:

- treatment of human carriers,
- treatment of cysticercotic pigs, and
- vaccination of pigs.

The other three are more appropriate as components of long-term programs or have a supportive value in short-term control projects:

- improved sanitation,
- changes in pig husbandry, and
- higher levels of general education.

The prevention strategies must rely on multiple approaches, tailoring each to the special features of the particular endemic area.

In 1992, a pilot project was launched in Ribeirão Preto, São Paulo, Brazil. The project included a number of environmental sanitation measures, meat inspection, monitoring of vegetable crops and commercial concerns, and active surveillance of taeniasis among food handlers.

**References**


