



Review Article

NEUROCYSTICERCOSIS: REVEALING THE FACTS OF A RARE DISEASE

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Article Received on: 11/11/14 Revised on: 03/12/14 Approved for publication: 18/12/14

DOI: 10.7897/2230-8407.0611**ABSTRACT**

Neurocysticercosis, a Central Nervous System disorder caused due to the infestation of the pork tapeworm *Taenia solium*, is characterized by seizures and headache most commonly, followed by certain other neurological symptoms. The disease is commonly diagnosed with neuro imaging techniques like CT or MRI. Treatment primarily involves symptomatic management with anti-epileptic medication and a combination of anti-parasitic and anti-inflammatory therapy, surgery is done in necessary cases. This is a preventable disease and further studies are underway to develop optimal treatment regimens and a vaccine against the parasite.

Keywords: Neurocysticercosis, *Taenia solium*, anti-parasitic therapy, seizure, Central Nervous System disorder.

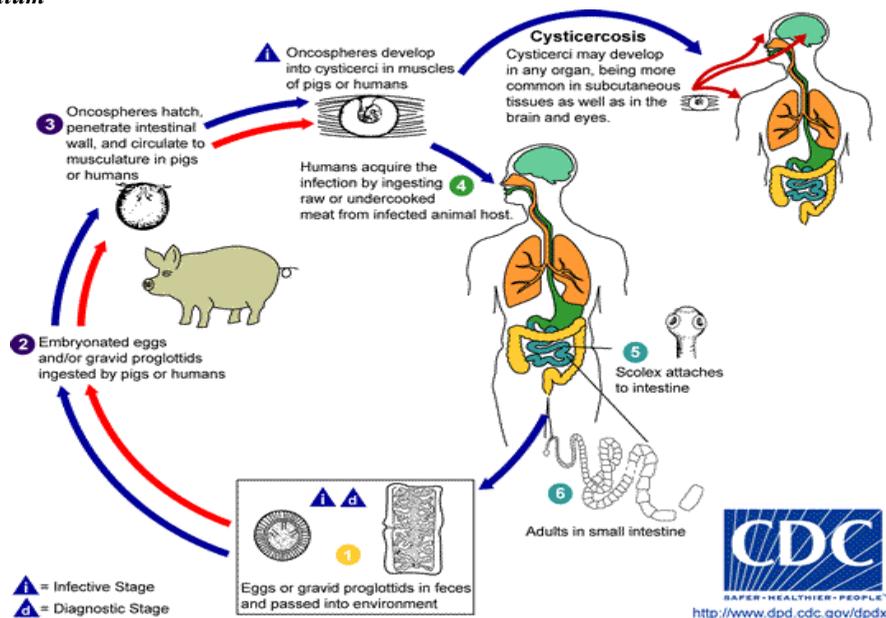
INTRODUCTION

Neurocysticercosis (NCC), a parasitic infection involving the Central Nervous System, results from the ingestion of undercooked pork or other food items contaminated by the eggs of the adult pork tapeworm, *Taenia solium*. It can either be parenchymal, the common form or extra parenchymal depending upon the site of infestation. While Parenchymal disease involves infection with cysticerci within the brain parenchyma, extra parenchymal disease ensues when cysticerci invade meningeal, subarachnoid, and intra ventricular space. Parenchymal NCC is characterized by the presence of active cysts in the brain and epileptic seizures. Extra parenchymal NCC possesses a poor prognosis due to its challenging diagnosis and treatment with clinical manifestations ranging from asymptomatic lesions to meningitis and hydrocephalus. Although it is a main disease of concern in the developing countries like India, Africa and

China with the exemption of the muslim population, increased migration has marked the spread of the disease to developed countries as well.¹ The World Health Organization (WHO) estimates that cysticercosis affects about 50 million people worldwide. Neurocysticercosis is a potentially eradicable disease and interventions to control are underway to eliminate this infection.²

Etiopathogenesis

T. solium has a two-host biologic cycle, where humans act as the definitive hosts carrying the intestinal tapeworm, and pigs as the normal intermediate hosts harboring the larvae or cysticerci. This parasite possesses a head (scolex) with 4 suckers and a double crown of hooks, an unsegmented neck and a large body with hundreds of hermaphrodite proglottids.³

Life cycle of *T. solium*

Life cycle of *Taenia solium* consists of six main steps

Step 1: Infected humans (definitive hosts) excrete the eggs or gravid proglottids through the feces onto nearby vegetation that when ingested by pigs subsequently develop into cysticerci in any organ more commonly in subcutaneous tissues as well as in the brain and eyes. Fecal oral contamination can result in autoinfection in humans which results in the re entry of *T. solium*

Step 2: Pigs (intermediate hosts) acquire the infection by eating the parasitized vegetation.

Step 3: Once the eggs are ingested, they migrate to the intestine and develop into oncosphere (hexacanth embryos) which invade the intestinal wall and lodge in the muscles of the pig and later develop into cysticerci.

Step 4: Humans are infected by eating undercooked or raw meat of an infected pig.

Step 5, 6: Cysticerci migrate to the small intestine and attaches to the intestinal wall using its scolex. Adult tapeworm develops normally within 2 months and can remain in the small intestine for several years.⁴

Most cysticerci emerge from the intestinal wall through mesenteric vessel and lodge in the grey white cortical junction of the brain parenchyma, ventricle, meninges, encephalon, subarachnoid space and eyes.⁵ The parasite has various immune protective mechanisms that help it to remain asymptotically in the host tissue for prolonged duration. The parasite releases various glyco conjugates that produce a suppressive and immune regulatory environment that protects the parasite from inflammatory response. The cyst can either be single or multiple parenchymal that are seeded throughout the brain parenchyma or the third kind being multiple cerebral parenchymal cysts with secondary complication arising from neuronal damage, cerebral abscess and ventricular dilatation that can pave way to cerebral atrophy. Intra ventricular and meningeal cyst occludes the CSF channels causing obstructive hydrocephalus manifesting as headache, dementia and seizure. The CNS invasion of cysticerci induces an inflammatory reaction to meninges, encephalon and vascular regions, resulting in meningo-encephalitis and vasculitis.⁶

Clinical Manifestations

The clinical presentation of NCC depends upon the location of the cysts with headache and seizure being more commonly witnessed in people with parenchymal cysts whereas increased intracranial pressure (nausea, vomiting and headache) and impaired mental status are seen in the extra parenchymal disease. Less observed findings include mass effect, visual abnormalities, focal neurologic deficits and meningitis.

Parenchymal NCC

- Seizures may be focal, focal with secondary generalization, or generalized.
- Headaches are common and may be migraine like or tension-type.
- Neuro cognitive deficits, while rare, may include learning disabilities, depression, or even psychosis

Extra parenchymal NCC

- Most patients present with headaches or symptoms of hydrocephalus.
- Symptoms of increased ICP may include headache, nausea or vomiting, altered mental status, dizziness, and decreased visual acuity due topapilledema.
- Patients with numerous cysticerci in the basilar cisterns may present with communicating hydrocephalus, meningitis

(without fever), symptoms of lacunar infarcts due to small-vessel vasculitis, or symptoms of large-vessel infarcts due to cysticercal erosion into major arteries or severe inflammation of those arteries.

- Patients with spinal cysticerci typically present with radicular symptoms, but rarely with motor or sensory deficits traceable to a spinal level.
- Patients with ocular cysticerci report visual changes.

Spinal cord involvement

- Radiculopathy
- Myelopathy

Others

- Meningoencephalitis
- Stroke
- Subcutaneous nodules
- Ocular cysts^{5,6}

Diagnosis

Clinical presentation and radiographic imaging is the cornerstone of diagnosis of NCC. The diagnosis should reasonably begin with Computed Tomography (CT) and serology with Enzyme-linked immune electro transfer blot assay (EITB) or Magnetic Resonance Imaging (MRI) of the brain, with MRI required only in cases where CT is indecisive. EITB can be performed on both serum and CSF with higher specificity on serum. Patients suspected of having basal subarachnoid NCC are candidates for spine imaging also. However, CT is inferior to MRI in detecting spinal lesions. Cerebral cortex or brainstem is the site of invasion by cysticerci in cases of parenchymal neurocysticercosis, with simultaneous cystic and calcified lesions. Involvement of the brainstem, basal ganglia or cerebellum, mass effect, diffuse cerebral edema, cerebral infarction, giant cells measuring > 20 cm and multiple cysts numbering > 50 are less likely yet rare manifestations of parenchymal NCC. In case of extra parenchymal NCC, cerebral imaging may be helpful in finding intra ventricular or subarachnoid cysts, leptomeningeal enhancement, or hydrocephalus with ventricular enlargement. Ocular and extra ocular muscle infestation can also be identified using CT. Serological tests detect cysticercal antigens or anti cysticercal antibodies with the preferred test for the detection of antibodies being EITB and a number of newer assay methods are in the pipeline. Studies of monoclonal antibody based ELISA tests for detection of parasite antigens have demonstrated detection of circulating and CSF antigen and may be useful for both diagnosis as well as post therapeutic monitoring. Other assays which are coming up include antigen detection tests to detect live parasites and polymerase chain reaction assays. Antigen detection tests are more sensitive with CSF. Fundoscopic examination allows direct visualization of the parasite and should be carried out in all patients to rule out ocular cysticercosis. CSF studies in a patient with parenchymal lesions show mild leukocytosis with normal glucose and protein concentrations while active arachnoiditis or ventriculitis present with pleocytosis and elevated protein concentrations and decreased glucose concentration. Blood culture may show peripheral leukocytosis, eosinophilia and an elevation in erythrocyte sedimentation rate (ESR). A decrease in N-acetyl aspartate (NAA) and creatinine levels and elevated lactate and metabolites such as alanine and succinate have also been reported. Brain biopsy may be required only in those cases in which the other non-invasive tests fail to bring out a diagnosis. For extra neural cysticercosis, excisional biopsy of a skin or muscle lesion may be helpful in establishing a diagnosis. Intestinal taeniasis is very common in patients with cysticercosis. Carriers of the worm can be picked up through the examination of the stool. Specific co-pro antigen detection by ELISA and PCR can be employed for screening of carriers in endemic areas. The conditions that are sometimes misunderstood for NCC include primary or metastatic tumor of the brain, pituitary, glioblastoma, tuberculoma, brain abscess,

toxoplasmosis, nocardiosis, other parasitic/fungal infections or even stroke.⁷

Treatment

The initial approach to patients with clinical manifestations of neurocysticercosis (NCC) should primarily focus on management of symptoms such as seizure control with antiepileptic drugs and treatment of increased intracranial pressure, if present. Subsequently a combination of anti parasitic and anti-inflammatory therapy is employed. Surgery is also done in necessary cases. Treatment also depends on the location and number of cysticerci, and the stage of cyst development.⁸

Antiepileptic therapy

Antiepileptic drugs should be administered to patients with NCC who present with seizures. The drugs commonly used for this purpose include phenytoin or carbamazepine. Newer therapies like levetiracetam or topiramate are likely to be at least as effective, perhaps better tolerated, but are more expensive. Antiepileptic therapy may also be initiated in patients who do not present with seizures but who are at high risk for seizures. The risk of seizures appears to be highest in the setting of multiple lesions, particularly when the lesions are degenerating and are surrounded by inflammation. An otherwise asymptomatic patient is not generally considered for prophylactic antiepileptic drug therapy. Seizures most often recur for months and may indefinitely recur. Anticonvulsant medications must be continued until cysts have resolved and until the patient is seizure free for 1-2 years.

Anti parasitic drugs

The most commonly used anthelmintic agents include Albendazole, orally administered at a dose of 15 mg/kg/day divided into 2 daily doses for 8-30 days (not to exceed 800 mg/d in children or 400 mg twice daily in adults).⁸ Less commonly Praziquantel, is orally administered at a dose of 50-100 mg/kg/d divided into three daily doses for 30 days. Albendazole is generally preferred over praziquantel because of its higher eradication rate of parenchymal brain cysts. More prolonged treatment courses (e.g. 30 days of albendazole, which may be repeated) may be needed for extra parenchymal or extensive disease. These anti parasitic medications are effective in eliminating viable cysticerci though they may cause reactive localized inflammation. Consequently, the use of these medications must be evaluated on a case-by-case basis. More than one course of treatment may be necessary to completely eliminate active cysts. In all patients with multiple cysts and associated cerebral edema (cysticercal encephalitis) anti parasitic therapy should be continued until the cerebral edema is controlled by corticosteroid therapy. In addition, anti parasitic drug therapy may cause permanent damage if used to treat ocular or spinal cysts, even when combined with corticosteroids. A careful ocular examination should be done prior to commencement of anti parasitic drug treatment to rule out ocular cysts.^{9,10}

Anti-inflammatory medication

Corticosteroids are frequently used in patients with neurocysticercosis. The mostly used drug is Dexamethasone at doses between 4.5 and 12 mg/day. Prednisone at 1 mg/kg/day may replace dexamethasone when long-term steroid therapy is required. Corticosteroids are frequently used to decrease neurological symptoms due to the death of the parasite and are the primary management for chronic cysticercosis arachnoiditis or encephalitis, where up to 32 mg of dexamethasone per day is needed to reduce the brain edema accompanying this condition. Mannitol at doses of 2 g/kg/day is also used for acute intracranial hypertension secondary to neurocysticercosis.^{11,12}

Surgery

Surgical management may also be necessary in some selective cases of cysticercosis. Surgical removal of central nervous system cysts or placement of a ventriculo-peritoneal shunt (to relieve pressure) or ventriculostomy for CSF diversion is at times necessary in some cases of neurocysticercosis.^{13,14} Certain cases of cysticercosis involving the eyes or subcutaneous cysts may also require surgery. Neuro endoscopy may be used to remove certain ventricular cysts and open resection though rarely performed, is unavoidable in patients with giant cysticerci with life-threatening mass effect, cysticerci lodged in the fourth ventricle or nearby vascular structures or sites out of reach of flexible endoscopy.¹⁵

Prevention and control

- Since ingestion of undercooked meat is the main cause of the disease, consuming properly cooked food is one among the main ways to prevent catching the disease.
- Washing hands with soap and warm water after using the toilet, changing diapers and before handling food is one way to prevent the disease.
- Teaching children the importance of washing hands to prevent the infection is important.
- Washing and peeling all raw vegetables and fruits before eating.
- Good food and water safety practices while travelling in developing countries should be followed.
- Drink only bottled or boiled water.
- Filter unsafe water through an absolute 1 micron filter and dissolve iodine tablets in the filtered water.^{16,17}

CONCLUSION

Neurocysticercosis is a very common parasitic infection of the CNS and the main reason for acquired epilepsy in the developing countries. It is caused by the accidental ingestion of pork tapeworm *T. solium*. The clinical presentation varies depending on the larval lodging and host immune responses. Management is aimed at symptomatic control and the eradication of the parasite. Neurocysticercosis is potentially eradicable, and control interventions are underway to eliminate this infection. Further study is going on to fully clarify the optimal treatment regimens for cysticercosis. Future strategies may mainly focus on prevention of the spread of *T. solium*. A report from the Centers for Disease Control and Prevention Working Group on Parasitic Diseases classified cysticercosis as a potentially eradicable disease. Efforts may include decreasing pork tapeworm carriers and thus reducing *T. solium* egg shedding through more intense meat inspection and preparation, eliminating exposure of pigs to human feces and developing a vaccine against *T. solium*.

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- Cite this article as:**
Lakshmi R, Amrutha V Ajai, Aditi K. Neurocysticercosis: revealing the facts of a rare disease. *Int. Res. J. Pharm.* 2015; 6(1):1-4 <http://dx.doi.org/10.7897/2230-8407.0611>

Source of support: Nil, Conflict of interest: None Declared