Review Article

Neurocysticercosis

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Introduction

Neurocysticercosis is the most common parasitic disease of the central nervous system. Human acquire cysticercosis by the ingestion of food contaminated with the egg of tapeworm Taenia solium. Neurocysticercosis is distributed world wide and is endemic in the developing world especially most of Asia and Africa. In Nepal over 80% of cases of young individuals presenting with seizure disorder are diagnosed as heaving neurocysticercosis. In countries where disease is endemic, cysticercosis may effect 2–4% of general population. Sero-epidemiological studies in India have demonstrated that approximately 2–3% of general population have anticysticercal antibodies in their serum. The disease has also become increasingly recognized in developed countries because of immigration from countries where the disease is endemic. Recently neurocysticercosis was found in ten percent of patients with seizures presenting in Los Angeles and in six percent of such patients in New Mexico. Disease is most prevalent in areas with poor sanitation, lack of proper water supply and sewage system.

Pathogenesis:

Disease is caused by the larval from of Taenea solium. Humans are the only definitive host and harbour adult tapeworm which is 2–8 meters in length in the intestine. The worm is attached to the mucus of the small bowel by several pairs of scolex. Terminal egg bearing segments or proglottids are periodically discharged in the stool. After ingestion by the pigs which are the intermediate hosts, eggs develop into hexacanth larvae called oncospheres which penetrate the small bowel of pig and are deposited throughout the body of the pig, especially in the skeletal muscles. The oncosphere then develop into cysticercal stage. When humans consume ill cooked pork, the cysticercal larvae develop into adult tape worms. It was previously assumed that cysticercosis is aquired mainly by eating ill cooked or raw pork. It is now obvious that in cysticercosis can be acquired through faecal–oral route by consuming contaminated food e.g. raw vegetables or water. So the disease can occur in both vegetarians and non vegetarians.

Cysticerci may be found in almost any tissue. Most frequently cysts may be located in the brain, subcutaneous tissue, muscles, eyes and rarely in spinal cord and other tissues in the decreasing order of frequency. Possibly because of the limited immune system in the central nervous system parasites survive most frequently in the nervous system. In the brain, cysticerci are located mainly in the parenchyma of cebral cortex, the sub-arachnoid space or in ventricular system. Cerebral cysticerci are usually located in gray matter or at the junction of the gray and white matter. Cysticerci may be single or multiple in the brain and are usually about 1cm in diameter but may be as large as 5cm.

Cysticerci evolve through different stages. In the earlist stage so called 'vesicular stage', it has a thin friable translucent membrane and there is an invaginated larvae inside the cyst. Second stage is called 'colloidal stage'. In this stage cyst shows hyaline degeneration and minaralisation. As the time advances cyst begins to reduce in size, wall become thicker and the contents are transformed into coarse granules. This is called 'granular-nodular' stage. Ultimately the cyst becomes completely mineralized, the 'calcified' stage. These different stages of cyst produce corresponding CT scan pictures. Intact cysticerci provoke minimal immunological reactions. Degenerating cysticerci produces more pronounced inflammatory response. Subarachnoid cysticerci may be small and scattered or may from large clumps and cysts may produce tumour like effects. Inter ventricular cysts are usually single and tend to lodge in the fourth ventricle but can be present in the third or lateral ventricles. These intraventricular cysts produce granular ependymitis as well. An unusual 'racemose' form of cysticercus may be seen in the

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subarachnoid space or in the ventricles. These grape–like multilobulated cysts are usually sterile (lack scolex) and cause marked adhesive arachnoiditis and obstructive hypnocephalus.

About 20% of human cysticercosis cases show an ocular involvement. Ocular cysticerci is seen most commonly in the vitrous humor and subretinal tissue. It can be seen in extra-ocular muscles, anterior chamber and conjunctiva. Host reaction to cysticerci in eye vary from slight to severe inflammation and can cause retinal detachment, chorioetinitis and iridocyclitis. In the skeletal muscles larvae go through similar but more rapid morphological changes, such that the parasite may be alive in the brain but calcified and dead in the muscles.

Incubation period between infection and clinical presentation is variable. It may be less than a year to 30 years, the average interval being 5 years.

Clinical Presentation:

Over 90% patients with paranchymal brain involvement present with seizure disorder. Most of the patients have partial seizure with or without secondary generalization. Other neurological symptoms are relatively uncommon and include chronic headache, nausea, vomiting, visual changes, focal neurological signs, mental status changes and tremors.

Physical examination usually reveal nonfocal neurological findings. Papilloedema with decreased retinal venous pulsation suggest raised intracranial pressure. Sometimes nystagmus or visual field defects, intraocular larvae, subcutaneous nodules and muscular pseudohyoertrophy can be found in these patients. Neurocysticercosis can manifest as focal neurological deficit of vascular origin. It is usually caused by inflammatory occlusion of the cerebral arteries secondary to cysticercotic arachnoiditis. Mostly, the small penetrating vessels are involved producing lacunar infarcts. Major vessels like middle cerebral artery can be involved producing larger infacts. In any young individual presenting with stroke from an endemic area possibility of neurocysticercosis as a causative factor should always be considered. Disseminated intraparanchymal form of neurocysticercosis can present as acute encephalitis especially in young children and adolescents. Symptomatic disseminated neurocysticercosis manifests with frequent seizures, dementia, muscular pseudohypertrophy, localizing signs and intracranial hypertension.

Spinal cord is involved in about 2% cases. Spinal cysticerci many mimic intraspinal tumours. Intramedullary cysts cause symmetric or asymmetric paraparesis and a transverse sensory level.

Diagnosis:

Diagnosis of neurocysticercosis can be made from histopathological examination, imaging techniques and serological tests. The histological examination of the materials obtained form a tissue containing cysticercus larva makes the definitive diagnosis of cysticercosis.

Imaging:

Plain x-ray of skull and limbs may show Cigar-shaped calcification.

CT scan is the most useful diagnostic procedure in the diagnosis of neurocysticercosis. The CT finding depends on the number, location and stage of the lesion. In the vesicular stage, cysts appear circumscribed and hypodense. These lesions do not enhance after contrast administration and the surrounding oedema may be absent or minimal. In the collidal stage, which represents a dying cyst, there is a ring enhancing lesion surrounded by oedema. On the nodular–granular stage noncontrast CT shows hyperdence lesion. Small single enhancing CT lesions are the commonest findings in patient with neurocysticercosis. The CT lesions are usually more than 20mm in size, well defined and are most frequently located in paneto-occipital region.

CT scan in sub-arachnoid neurocysticarcosis may show hydrocephalus secondary to inflammatory occlusion of Luschka's and Magendie's foramen, abnormal enhancement of tentorium and basal citerns due to arachnoiditis, brain infract due to cysticarcotic endarteritis. The intraventricular from of cysticercosis present as rounded areas of low density in CT scan that deform the ventricular system and interfere with CSF circulation.

MRI is generally better than CT scan for the diagnosis of neurocysticercosis. MRI is about four times more sensitive than CT scan in the detection of cysts in brain stem, subependymal location, cerebellum, subarachnoid space, spinal cord and inside the ventricles. MRI shows living paranchymatous cysts as rounded lesions of CSF equivalent density in both T1 and T2 weighted images. An isodense or hypodense scolex can be identified within the cyst producing 'pea in the pod' appearance. However CT scan is better is detecting calcified cysts.

Serological Test:

ELISA test is the most commonly used serological test in our part of the world. ELISA test on serum is unreliable as it can give significant number of false positive or negative results. ELISA on CSF is 87% sensitive and 95% specific and remains as a useful supportive tool for the diagnosis.

Enzyme–linked immunoelectrotrasfer blot assay (EITB) is the most reliable serological test in serum. It has specificity 100% and sensitivity up to 94 to 98% for patients with two or more cystic or enhancing lesions. But in patients with single lesion, EITB can give false negative results. Sensitivity and specificity of this test is low in patients with calcified lesions as well.

Depending upon the clinical, radiological immunological and epidemiological parameters diagnostic criteria for cysticercosis had been established by experts which has seen been periodically modified. However, these criterias can not be fulfilled in most of the patients from Indian subcontinent.

Revised diagnostic criteria of neuro-cysticercosis (Del Brutto) et al.

Absolute criteria :

1. Histological demonstration of parasite.
2. CT or MRI showing cystic lesion with scolex.
3. Fundoscopic visualization of parasite.

Major criteria :

1. Lesions suggestive of neurocysticercosis on CT or MRI
2. Positive serum EITB.
3. Resolution of cyst after therapy.
4. Spontaneous resolution of single enhancing lesion.

Minor criteria :

1. Lesions compatible with neurocysticercosis on CT or MRI.
2. Suggestive clinical features.
3. Positive CSF ELISA
4. Cysticercosis outside CNS

Epidemiological Criteria :

1. Household contact with T. solium infection.
2. Immigration from or living is on endemic area.
3. Travel to an endemic area.

Definite : One absolute; or two major + one minor + one epidemiological criteria.

Probable : One major + two minor; one major + one minor + one epidemiological; three minor + one epidemiologic.

Treatment:-

Treatment of neurocysticercosis includes:

a. Control of seizure
b. Anti parasitic drugs
c. Anti inflammatory drugs
d. Surgery

Control of seizure:

Seizure control plays the pivotal role in the treatment of neurocysticercosis. Seizure control can be achieved by one first line antiepileptic therapy in most of the cases. If seizure control is not satisfactory (i.e. more than two seizures in a period of six months) dosage of antiepileptic therapy should either be adjusted or the therapy should be changed to a different antiepileptic drug. Patients who have no active lesions (cyst or enhancing lesions on CT or MRI scan) six months after treatments show better seizure control. After one seizure free year the drug dosage should be tapered over a two month period and stopped then after. In some patients, seizures can reccur after dose

reduction or withdrawal of antiepileptic therapy, and some may require long term antiepileptic therapy.

Antiparasitic drugs:-

Two drugs praziquintal and albendazole are effective against cysticercosis. Before the introduction of these two medications in 1980, brain surgery was the only therapeutic approach to neurocysticercosis. Both agents frequently eliminate all the cysticerci in the brain. Albendazole has also been found to be effective against gaint parachymal, subarachnoidal intraventricular and even the spinal form of cysticercosis and frequently obviates the need of surgery. Initially longer courses of albendazole and praziquiental had been advocated. Now even the shorter treatment regimens are found equally effective. Complete course of praziquiental can be administrated in a single day (75–100 mg/kg body weight in 3 dose at 2 hour interval) with comparable efficacy instead of conventional treatment in 15 days. Similarly, one week therapy of albendazole is as effective as 30 days regimen.

There are many controlverses regarding anticyticercal treatment in neurocysticercosis. Opponents of anticysticercal therapy argue that:

1. Treatment is unnecessary since most cysts die by themselves within a short period and the effectiveness of the therapy is possibly a reflection of natural course of the disease.
2. Sudden destruction of parasites may trigger an inflammatory reaction that precipitate seizures and transient neurologic effects mainly headache and vomiting.
3. The long term prognosis of the under lying seizure disorder may worsen because of increase scarring due to acute inflammation.

A randamized trial conducted by Hector H. Gracia et al for the cysticercosis working group in Peru published in Jan. 2004 showed that in patients with seizures due to viable paranchymal cysts antiparasitic therapy decreases the burden of parasites and is safe and effective, at least in reducing the number of seizure with generalization. This study did not support any of the major arguments against the use of antiparasitic therapy.

It most be noted that most of the patients with neurocysticercosis present with single lesion. These single lesions spontaneously disappear within 6-12 weeks. That is why some authorities are still reluctant to use antiparasitic therapy in these patients.

Antiinflammatory treatment:

Treatment with anticysticercal therapy has been associated with high frequency of transient adverse reaction that seems to be due to the host's inflammatory reaction to dying parasites Corticosteroids have been recommended routinely along with anticysticercal therapy to reduce acute inflammatory changes during anticysticercal therapy. However, there is no controlled trial to support this practice. Patients with disseminated lesion should be treated with steroids only.

Surgical treatment:

Patients with intraventricular or subarachnoidal cysts presenting with hydrocephalus may require shunting procedure. It is usually advisable that a ventricular shunt be planned in all patients with subarachnoid cysticercosis before starting medical treatment. But the rate of shunt failure is high because of frequent shunt occlusion and infection. In patient with racimose and large cysternal cysts surgical treatment is usually required and is usually done by endoscopic procedure with good success.

Conclusions:

Neurocysticercosis is a complex disease condition. This is a preventable disease and appropriate health measure should be ensured for the effective prevention of the disease. Radiological improvement after treatment may not equate with satisfactory clinical outcome. The recent cranial trial shows that expeditious elimination of parasite is beneficial and cysticidal treatment should be administered to all patients with active parenchymal neurocysticercosis.

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