REVIEW ARTICLE

Neurocysticercosis : Current Vitae

Rajesh Sharma, Rupali Bargotra*, Vishal R Tandon,
S K Gupta***, Sourabh Verma***, J B Singh*****

Introduction

Neurocysticercosis is the most frequently observed parasitosis of the central nervous system worldwide. It is a compmon cause of neurological disease in developing countries and a major cause of epilepsy worldwide. Neurocysticercosis presents a peculiar problem, as it is an endstage infection, accidental in man, with a benign natural course and would have merited considerably less attention, had it not chosen to infest the brain (1). Humans are the only definitive hosts for T. Solium; Pigs are the usual intermediate hosts, although dogs, cats and sheep may harbour the larva forms. Humans acquire infection by ingesting under cooked pork containing cysticerci or from fecally contaminated food (2).

Clinical Manifestations

Intestinal infection with T. Solium may be asymptomatic. The target organs of tapeworm cyst are brain, eye and spinal cord. A unique characteristic of human neurocysticercosis is that the living parasite is very well tolerated in human brain, so symptoms and clinical disease primarily result from death of the organism and accompanying inflammatory reaction in the human CNS. When inflammation surrounds cysticerci in the brain parenchyma, seizures are frequent. These seizures may be generalized, focal or Jacksonian. Hydrocephalus results from obstruction of CSF flow by cysticerci and accompanying inflammation. Signs of raised intracranial pressure are often evident. Patients with hydrocephalus may develop papilloedema or altered mental status. If cysticerci develop at the base of the brain or subarachnoid space, they cause meningitis or arachnoiditis (2).

Diagnosis

The diagnosis of neurocysticercosis has greatly improved by introduction of computed tomography (CT) and magnetic resonance imaging MRI (3). These techniques demonstrate the number and topography of lesions, their stage of involution, and the degree of inflammatory reaction of the host against the parasites and have largely replaced previous radiological procedures such as plain roentgenograms, pneumoencephalograms, cerebral angiography and myelography. In general, MRI provides better image, detection and definition. The possibility of multiplanar reconstruction of images, its capability to visualize the posterior fossa without bone artifacts, and its high contrast resolution (far superior to that of CT) allow MRI to recognize many forms of cysticercosis not visualized on CT. However, the cost of MRI is high and the equipment is scarcely available in many endemic countries, and its sensitivity for the detection of calcified lesion is poor. CT remains the best screening neuroimaging procedure for patients with suspected neurocysticercosis, and MRI is the imaging modality of choice for the evaluation of patients with intraventricular cysticercosis, brainstem cysts and small cysts located over the convexity of cerebral hemispheres. MRI is also superior to CT in the follow-up of the patients after therapy. Noninvasive MR cisternography with fluid attenuation inversion recovery after 100% supplemental oxygen is the latest technique for noninvasive imaging of the subarachnoid space (4).

The development of improved immunodiagnostic tools has also contributed to the knowledge on the

From The Postgraduate Departments of Radiagnosis, *Pathology, **Pharmacology & ***Medicine, Govt. Medical College, Jammu.
Correspondece to: Dr. S. K. Gupta, Associate Professor & Neurologist, Department of Medicine, Govt. Medical College, Jammu (J&K).

importance of taeniosis/cysticercosis by enabling sero-epidemiological surveys and community-based studies (5). Immunodiagnostic techniques include detection methods for specific antibodies and for circulating parasite antigen in serum or cerebrospinal fluid. The antigens used in immunoblot and enzyme-linked immunosorbent assay (ELISA) for antibody detection have been evolved from crude extracts to highly purified specific fractions and recombinant antigens of the glycoprotein family, increasing both the sensitivity and the specificity of the tests. The applicability of indirect immunofluorescent antibody test (IFAT) was compared with enzyme-linked immunosorbent assay (ELISA) in sera from 163 cases of confirmed neurocysticercosis, 101 other neurologic and parasitic diseases and 100 normal controls in one study (6). As antigen, frozen sections of a Taenia solium metacestode from a human brain was used in IFAT and cystic fluid was used in ELISA, for the detection of specific IgG antibody, IFAT was equally sensitive (89.6%) and specific (85.1%) as ELISA. The antibody titers by IFAT were correspondingly increased with mean absorbance of ELISA. The corresponding rate of positivity in the two techniques was 90.8%. Except for the difficulty in detecting antibodies in cerebrospinal fluid, IFAT was concluded to be very useful for the serodiagnosis of human neurocysticercosis. To determine the source of cysticercus-specific IgG antibody in cerebro-spinal fluid, paired samples of serum and CSF were collected from confirmed neurocysticercosis, other neurologic diseases and normal control in another study (7). The antibody levels in serum and CSF were measured by enzyme-linked immunosorbent assay (ELISA). With the measurement of total protein, albumin and IgG concentration in serum and CSF, the contribution of IgG in CSF were calculated in transudation, exudation and intracranial synthesis. Mean concentrations of total proteins, albumin, IgG and proportional IgG levels in CSF by transudation, exudationcand-intracranial synthesis were elevated in neurocysticercosis. But only the intracranial synthesis of IgG showed a statistically significant correlation with the specific IgG antibody levels in CSF. In CSF from lateral ventricle in the 4th ventricular neurocysticercosis, the protein concentrations were normal and the specific antibody levels were negative. However, in consecutively secured lumbar CSF from the same patients, the former were increased and the latter were positive. These results indicated that, in neurocysticercosis, the specific IgG antibody in CSF was a local product of intracranial synthesis.

The application of ELISA for the detection of circulating parasite antigens may present some diagnostic advantages since it demonstrates not only exposure but also active infections. Symptoms in NC usually occur when cysts enter into a degenerative phase associated with perilesional inflammation. A study has speculated that neuron-specific enolase (NSE)-a marker of neuronal injury-could be elevated in patients with degenerating cysts comparing to those with viable cysts (8). Further use of neuron specific enolase for assessing the severity and outcome in patients with neurological disorders is also being studied (9).

Until now only a few of the current techniques have been standardized and fully validated, making comparisons between studies difficult. The lack of a gold standard is a serious drawback. In surveys on cysticercosis, antibody detection systems have been useful in identifying the risk factors associated with transmission of Taenia solium; a high seroprevalence in a community indicates a “hot spot” where preventive and control measures should be applied. In contrast, the potential use of immunodiagnostic tools to identify cases of neurocysticercosis (NCC) in man is subject to debate. The correlation between a positive serology and neurological symptoms and/or lesions indicative for NCC on neuro-imaging techniques is poor to fair in most studies. This may be explained by the unpredictable clinical outcome of the infection and the variable immunological response of the human host to infection. A major problem is that in many developing countries, neuro-imaging methods are inaccessible and/or too expensive for the rural population at risk. Under these conditions, serology may provide the only tool for diagnosis of the infection.

Table 1. Proposed diagnostic criteria (10)

Absolute criteria
· Histologic or microscopic demonstration of cysticerci in biopsy material
· Visualization of the parasite in the eye by fundoscopy
· Neuroradiological demonstration of cystic lesions containing scolex
Major criteria
· Neuroradiologic lesions suggestive of neurocysticercosis
· Demonstration of antibodies to cysticerci in CSF by ELISA
· Cigar shaped calcification in soft tissue on X-ray
Minor criteria
· Subcutaneous nodules suggestive of cysticerci
· Punctate calcification on radiographic studies
· Clinical manifestations
Suggestive
· Disappearance of lesion during treatment
Epidemiologic Criteria
· Residence in endemic area
· Frequent travel to endemic areas
· Household contact

Treatment

Disease manifestations due to neurocysticercosis vary markedly and depend upon the location, size and number of cysts as well as viability or degeneration of cysts and presence, type and degree of host response. Accordingly the clinical management for each patient should be individualised (11). The medical modalities of treatment include drugs to control seizures, antiparasitic drugs and steroids. Surgery has a limited role to play in the management.

Medical Management (2,12)

Management is primarily symptomatic. Anticonvulsants are given for seizure control which are discontinued after two years if parenchymal lesions resolve without calcification and patient remains seizure free.

Antiparasitic Drugs

These drugs achieve faster resolution of neuro-radiologic abnormalities though some trials have failed to identify any clinical advantage for parenchymal lesions. Common drugs in use include praziquantel and albendazole. Praziquantel is instituted 50-60mg/kg daily in three divided doses for 15 days or 100mg/kg in three doses given over a single day. Albendazole (15mg/kg/day) is given for 8 to 28 days. Both the drugs, by increasing inflammatory response around dying parasite, may increase seizures or hydrocephalus (13,14). A recent study has indicated that granulomas replace cysticerci that have resolved spontaneously more often than they replace cysticerci that have been destroyed by medications (15). Studies also suggest that patients with single ring enhancing lesions do well regardless of antiparasitic therapy (16).

Role of Steroids (11)

High dose glucocorticoids can be used during treatment or if symptoms worsen. Steroids induce first pass metabolism, thus should be used with caution with praziquantel. They are also given to patients with subarachnoid cysts or giant cysticerci to reduce arachnoiditis and accompanying vasculitis. They also have a good role to play in patients with cerebral edema and elevated intracranial pressure due to multiple inflammed lesions where antiparasitic drugs are avoided.

Surgical Management (11,17)

Surgery usually has a role in emergent reduction of intracranial pressure in case of obstructive hydrocephalus. This can be achieved by endoscopic surgery or by a diverting procedure such as ventriculo-peritoneal shunting. Few patients have also been subjected to open craniotomy to remove cysticerci, but this procedure is not done frequently.

Prevention & Control

Neurocysticercosis due to Taenia solium infection is an important cause of human morbidity and mortality. Despite the availability of effective anthelmintics, the disease remains prevalent in many parts of the world and there is a need for new and improved measures for control of the infection. An effective vaccine to prevent infection in pigs, the parasite's natural intermediate host, would be a valuable new option to assist with T. solium control. Several approaches are being used currently towards the development of a T. solium vaccine and these approaches emphasize on the

use of recombinant oncosphere antigens. Highly effective vaccines have been developed against cysticercosis in sheep and cattle caused by Taenia ovis and Taenia saginata, respectively. This success has encouraged the adoption of a similar strategy for T. solium. The recent finding that one oncosphere antigen, TSOL18, can induce complete protection against T. solium infection in pigs, highlights the potential for development of a practical vaccine (18). An International collaborative efforts and commitment of both national and local authorities to control the disease needs to be convincingly solicited and, as for most zoonotic diseases, an interdisciplinary approach is essential to reduce global burden of neurocysticercosis (19).

References

1. Narula G, Bawa KS. Neurocysticercosis-New Millennium, ancient disease and unending debate. *Ind J Pediatr* 2003; 70(4): 337-42.
2. While Clinton, Weller PF. Cestodes. Taenia solium and cysticercosis. In: Braunwold E, Fauci A, Kasper DL, Hauser SL, Longo DL, Jameson JL (eds.). Harrisons Principles of Internal medicine 16th ed. Mcgraw Hill 2005. pp. 1273-76.
3. Garcia H, Del Brutto O. Imaging findings in neuro-cysticercosis. *Acta Trop* 2003; 87(1): 71-78.
4. Braga F, Rocha AJ, Gomes HR *et al*. Noninvasive MR cisternography with fluid attenuated inversion recovery and 100% supplemental 0_2 in the evaluation of neurocysticercosis. *Am J Neuroradiol* 2004; 25(2): 295-97.
5. Domy P. Immunodiagnostic tools for human and porcine cysticercosis. *Acta Trop* 2003; 87(1): 79-86.
6. Eom KS, Cho SY, Rim HI. Comparative evaluation of indirect immunofluorescent antibody test with enzyme-linked immunosorbent assay in serodiagnosis of human neurocysticercosis. *Kisaengchunghak Chapchi (Korea)* 1988; 26(1):27-32.
7. Cho SY. Intracranial synthesis of specific IgG antibody in cerebrospinal fluid of neurocysticercosis patients. *Kisaengchunghak Chapchi (Korea)* 1988; 26(1): 15-26.
8. Lima JE, Takayanagui OM, Garcia LV *et al*. Neuron-specific enolase in patients with neurocysticercosis. *J Neurol Scien* 2004; 217(1): 31-35
9. Lima JE, Takayanagui OM, Garcia LV *et al*. Use of neuron-specific enolase for assessing the severity and outcome in patients with neurological disorders. *Braz J Med Biol Res* 2004; 37(1): 19-26.
10. Del Brutto. Proposal for disgnostic criteria for human cysticercosis and neurocysticercosis. *J Neural Sci* 1996; 142: 1.
11. Nash TE. Human case management and treatment of cysticercosis. *Acta Trop* 2003; 87(1): 61-9.
12. Garcia HH *et al*. Current consensus guidelines for treatment of neurocysticercosis. *Clin Microbiol Rev* 2002; 15: 747.
13. Cutter AC. Prognosis for seizure recurrence in patients with newly diagnosed neurocysticercosis. *Neurology* 2003; 60(11): 1873-74.
14. Kumar Garg R. Risk of seizure recurrence in patients with neurocysticercosis. *Natl Med J India* 2003; 16(2): 90-1.
15. Hector H, Garcia E, Pretell J *et al*. A trial of antiparasitic treatment to reduce the rate of seizure due to cerebral cystecercosis. *N Eng J Med* 2004; 350: 249-58.
16. Riley T, White AC. Management of neurocysticercosis. *CNS Drugs* 2003; 17(8): 57791.
17. Zymberg ST, Paiva Neto MA, Gorgulho AA, Cavalheiro S. Endoscopic approach to fourth ventricle cysticercosis. *Arq Neuropsiquiatr (Brazil)* 2003 ;61(2-A):204-7.
18. Lightowlers MW. Vaccines for prevention of cysticercosis. *Acta Trop* 2003; 87(1): 129-35.
19. Engels D. The control of human (neuro) cysticercosis: which way forward? *Acta Trop* 2003; 87(1): 177-82.

GUIDELINES FOR ARTICLES TO BE SUBMITTED UNDER EACH CATEGORY TO *"JK SCIENCE"* JOURNAL OF MEDICAL EDUCATION & RESEARCH

Article Type	Summary: No. of Words	Key Words: No. of Words	Text : No. of Words	Sub-Headings	Tables: Max. No.	Figures: Max. No.	No. of References
ED	NR	NR	≤ 600-800	NR	NR	NR	≤ 10
RA	NR	NR	≤ 3000	Variable	2	2	30-35
OA	≤ 200	3-5	≤ 2000	Standard	4	2	20-25
SC	≤ 100	3-5	≤ 1200	Standard	2	1	10-15
CR	< 50	3-5	≤ 600-800	Standard	1	3	≤ 10
DR	NR	NR	≤ 1000	NR	1	1	≤ 10

ED = Editorial RA = Review Article; OA = Original Article; SC = Short Research Communication; CR = Case Report; DR = Drug Review