NEUROCYSTICERCOSIS IN SOUTH-CENTRAL AMERICA AND THE INDIAN SUBCONTINENT

A COMPARATIVE EVALUATION

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ABSTRACT - Neurocysticercosis is an important public health problem in South-Central America and South Asia. A review of the differences in epidemiological and clinical attributes of cysticercosis and taeniasis in South Central America and India, respectively, is undertaken in the present communication. Intestinal taeniasis is hyperendemic in several American countries. In comparison, the prevalence of Taenia solium infestation is lower in India. The clinical manifestations in several American neurocysticercosis series comprise epilepsy, intracranial hypertension and meningeal - racemose cysticercosis, in roughly equal proportions. An overwhelming majority of the Indian subjects present with seizures. The commonest pathological substrate of the disorder in Indian patients is the solitary parenchymal degenerating cyst. The reasons for the predominance of solitary forms in India, and of multilesional forms in South Central America are discussed. The magnitude of Taenia solium infestation and the frequency of pork consumption in a given population appear to influence the quantum of cyst load in affected individuals.

KEY WORDS: neurocysticercosis, taeniasis, epidemiology, clinical features, transmission.

Human cysticercosis occurs because of infestation with the larval stage of the pork tapeworm, Taenia solium. Man, the definitive host, harbours the adult tapeworm in his intestines. The pig is the intermediate host for the cysticercus larvae which develop from taenia eggs. Human cysticercosis occurs when man becomes an intermediate host because of autoinfection or food contamination by the taenid eggs. On account of the characteristic life cycle of the cestode, cysticercosis is common in developing countries, where sanitation is poor and the number of stray pigs is high. While cysticercosis was common in medieval Europe, it has been eradicated from developed countries leaving aside a few exceptions. The disorder is widely prevalent in Central and South America, parts of Africa and India and other South Asian countries. It is also being recognised with increasing frequency in Southwest United States, because of large scale Hispanic immigration. Several large series of neurocysticercosis have been reported from India and several countries in South and Central America. There appear to be certain differences between American and Indian reports with respect to the epidemiology, clinical manifestations and laboratory features of the disease. In the present communication, the author has tried to analyse the reasons for these differences.

Epidemiology: The geographic distribution of cysticercosis has been the subject of several reviews in the past. The prevalence of cysticercosis in a population is influenced by the prevalence of Taenia solium infestation. Therefore, it would be pertinent to review knowledge about

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the burden of *Taenia solium* infestation in South Central America and India. Until some time back, studies regarding the prevalence of taeniasis and cysticercosis were handicapped on account of the inavailability of specific, sensitive and economical screening tests for disease detection. Conventional methods for evaluating the community prevalence of taeniasis include enquiring for the passage of proglottides in faeces and microscopic stool examination for taenid ova or proglottides. A single, good coproparasitic examination would pick up less than half of the cases of intestinal taeniasis. Furthermore, microscopic examination does not differentiate between ova of *Taenia solium* and *Taenia saginata*. Therefore, the above methods do not provide accurate estimates of the burden of parasitic infestation. A newly developed technique, the inverted ELISA, has been found to be sensitive for the detection of taenia antigen in faecal samples. This coproantigen assay has been used as an epidemiological tool recently in Peru and Mexico. Flisser and coworkers in a preliminary application of the assay to a Mexican community found the prevalence to be one percent. Sarti et al., in another epidemiological survey of a rural Mexican village, using stool examinations, before and after praziquantel treatment, reported a prevalence of 0.9 percent. Authors from Brazil, have reported prevalence rates of 4 to 18 percent. Therefore, several South-Central American countries including Brazil, Mexico, Peru, Colombia, Ecuador and El Salvador, comprise hyperendemic zones for *Taenia solium* infestation. In India, a hospital based coproparasitic survey revealed taenia infestation in 2 percent of the patients attending either inpatient or outpatient departments. Such hospital based evaluations are likely to yield high prevalence rates, which cannot be extrapolated to the community. While accurate community based data are not available, it appears that India and several other Southeast Asian countries have a lesser prevalence of *Taenia solium* infestation in comparison to South-Central America. The lesser prevalence of taeniasis could be incidental to heterogeneous religious and cultural systems existing in India. Certain religions in India prohibit the consumption of pork or even other meats. Intestinal taeniasis should logically be infrequent in those religious communities which forbid pork consumption. However, in the slum dwelling poor communities in India, people often feed on stray pigs, which can be found around their habitations. Taeniasis should be common in such communities.

Neurocysticercosis is an important cause for symptomatic epilepsy in developing countries. In several recently published series of Indian patients with epilepsy, neurocysticercosis was implicated in 10-20 percent of cases. Nearly 70 percent of patients of epilepsy due to cerebral cysticercosis have a solitary cysticercus granuloma. Recent seroepidemiological studies in persons suffering from epilepsy in Peru and Mexico have revealed seropositivity rates of 15-29 percent. A Brazilian hospital based evaluation found evidence of neurocysticercosis in 33 percent of persons suffering from epilepsy. Patients with neurological involvement due to cysticercosis are commonly seen in large hospitals, both in America and India. Neurocysticercosis comprised up to 10 percent of neurological admissions in a large general hospital in Mexico. A diagnosis of neurocysticercosis was made in nearly 30 percent of brain pathology specimens processed after surgical excision in a Mexican hospital and in 2.5 percent of all space occupying lesions in a tertiary care centre in India. Incidental infestation with cysticercosis was noted in 2 percent of all autopsies performed in a hospital in Mexico.

Serological studies are convenient and economical methods for screening the community for cysticercosis. The indirect haemagglutination assay and ELISA have reasonable sensitivity, but false positive reactions can occur because of echinococcosis and schistosomiasis. The enzyme linked immunoelectrotransfer blot (EITB) assay, developed by Tsang and coworkers, overcame many of the drawbacks of indirect haemagglutination assay and ELISA. The immunoblot assay appears to be the most sensitive serological test for diagnosis of human cysticercosis. Sarti et al., in a serosurvey of a rural village in Mexico using the EITB assay, reported a seroprevalence of 4.9 percent. In the Indian subcontinent, the only application of the EITB assay, so far, has been to a group of patients with presumed solitary neurocysticercosis. Nearly 95 percent of the individuals in this series were seronegative. It is well known that seropositivity correlates with the number of
active lesions in the central nervous system\textsuperscript{21,28}. Hence individuals with solitary parenchymal cysts, particularly, the ones which are not in contact with the subarachnoid space may be seronegative. Nevertheless, it is difficult to explain the extremely low EITB positivity rates in the report from India\textsuperscript{36}. More studies using the EITB assay in Indian patients with single and multilesional neurocysticercosis are required. Community based seroprevalence using the EITB assay should also be determined in the Indian population.

**Clinical presentations:** Several large series of neurocysticercosis have been reported from Mexico, South America as well as South West United States\textsuperscript{21,28,47}. Salient clinical features in these series and their comparison with Indian reports are shown as in Table 1. An overwhelming majority of the patients in the reports from Southern United States orginally belonged to, or had history of travel to areas, hyperendemic for taeniasis. The dominant syndromes of neurocysticercosis in these patients were epilepsy, intracranial hypertension and cysticercal meningitis. Epilepsy occurred in 35-55 percent in the three representative series of patients. Intracranial hypertension was noted in 25-65 percent cases and meningitis in 42-48 percent cases\textsuperscript{21,28,47}. Several mechanisms are operative in the pathogenesis of intracranial hypertension in American patients. Inflammatory degeneration of a large number of parenchymal cysts can give rise to severe cerebral edema. This condition is known as cysticercoid encephalit\textsuperscript{37}. Raised intracranial tension may also be the result of either, obstructive or communicating type of hydrocephalus. Obstructive hydrocephalus in turn, could be a consequence of obstructing intraventricular cysts, third ventricular ependymitis due to degenerating intraventricular cysts, aqueductal stenosis because of perimesencephalic arachnoiditis and obstruction of the foramina of Luschka and Magendie due to meningeal fibrosis\textsuperscript{33,40}. A diagnosis of the third major syndrome of neurocysticercosis i.e. meningeal cysticercosis is based upon the presence of inflammatory cells in the cerebrospinal fluid (CSF) sediment or hydrocephalus or extracerebral racemose cysts\textsuperscript{5}. Meningismus and cranial nerve palsy are rarely encountered in cysticercal meningitis.

Dixon and Lipscomb\textsuperscript{14}, in their seminal communication on neurocysticercosis, reported clinical features in 450 cases among British soldiers posted in India. The authors noted that epilepsy occurred in up to 92 percent cases, whereas intracranial hypertension was seen in only 6 percent of their series. The proportion of cases with epilepsy vis-a-vis raised intracranial pressure was much more in comparison to their relative incidence in American reports. Experience in the post computerized tomography (CT) scan era, in India is similar\textsuperscript{12,52}. Epilepsy occurs in 71-94 percent and raised intracranial tension has been recorded in 12-30 percent cases\textsuperscript{12,52}. A study of CT findings in 58 Indian patients with neurocysticercosis, revealed that only two patients had ventriculomegaly\textsuperscript{12}.

<p>| Table 1. Comparative evaluation of clinical manifestations of neurocysticercosis in three representative series from Central America and United States and one series from India. |
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<table>
<thead>
<tr>
<th></th>
<th>McCormick et al.\textsuperscript{28} 1982</th>
<th>Grisolia and Wiederholt\textsuperscript{21} 1982</th>
<th>Sotelo et al.\textsuperscript{47} 1985</th>
<th>Venkataraman\textsuperscript{52} 1995</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of cases</td>
<td>127</td>
<td>17</td>
<td>753</td>
<td>228</td>
</tr>
<tr>
<td>Clinical manifestations</td>
<td></td>
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<tr>
<td>Epilepsy</td>
<td>70 (55%)</td>
<td>6 (35.3%)</td>
<td>395 (52.4%)</td>
<td>202 (79.2%)</td>
</tr>
<tr>
<td>Raised intracranial tension</td>
<td>48 (37.8%)</td>
<td>11 (64.7 %)</td>
<td>327 (43.4%)</td>
<td>32 (12.6%)</td>
</tr>
<tr>
<td>Meningitis</td>
<td>54 (42.5%)</td>
<td>*</td>
<td>326/694** (46.9%)</td>
<td>11 (4.3%)</td>
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*data not available; **based on the presence of inflammatory CSF (CSF was done in 694 patients only).
Similarly, evidence of meningeal involvement is uncommon in the Indian cases of neurocysticercosis. Meningeal cysticercosis accounted for 8 percent out of a total of 170 patients of neurocysticercosis seen in one army hospital in over a 15 years period. No case of racemose cysticercosis could be identified in this series. It appears, therefore, that the syndromes of intracranial hypertension and racemose-meningeal cysticercosis are uncommon in Indian patients when compared to their incidence in several American series. The reasons for this difference are not clear. The CSF abnormalities in cysticercal meningitis resemble those in tubercular meningitis, a condition that is fairly common in the Indian subcontinent. It may be possible that a certain proportion of persons with cysticercal meningitis are empirically diagnosed and treated as cases of tubercular meningitis. The presence of eosinophils in the CSF, which is highly suggestive of cysticercal meningitis, is often not sought for, in cases of chronic meningitis. The demonstration of eosinophils requires special stains such as the Wright's stain. These stains are not routinely performed in the CSF sediments of patients with chronic meningitis. Therefore it is quite possible that cysticercal meningitis is underdiagnosed in the Indian subcontinent.

Given that epilepsy is the predominant presentation of neurocysticercosis in India, it is reasonable to assume that parenchymal forms outnumber meningeal forms of cysticercosis. Of the parenchymal lesions, the commonest are the degenerating solitary parenchymal cysts. These single cysticercus cysts manifest on CT scans, as what are variously known as “disappearing CT lesions” “vanishing CT lesions” or more appropriately single, small, enhancing CT (SSECT) lesion. The SSECT lesions can be found in 10-20 of percent CT scans of Indian patients with focal or generalised epilepsy (Fig 1). The aetiology of these SSECT lesions was enigmatic till time some back. Studies of excision biopsies of such lesions have revealed that a cysticercus granuloma underlies the majority of the lesions. Current opinion links the overwhelming majority of the SSECT lesions to be forms of solitary parenchymal neurocysticercosis. Rajshekhar et al. proposed clinical and radiological criteria for recognition of the SSECT lesions due to cysticercal granulomas. These are: (a) clinical - focal seizures or focal seizures with secondary generalisation, no evidence of raised intracranial tension and minimal or no neurological deficit; and (b) radiological - single ring or disc shaped contrast enhancing lesion, size less than 20 mm, minimal or no surrounding edema, no midline shift.

While solitary degenerating parenchymal cysticercosis appears to be the most common manifestation of neurocysticercosis, it does not mean that multilesional forms of neurocysticercosis are not encountered in India. Wadia et al. described three patients with widespread, profuse active cysts in the brain parenchyma and muscles under the rubric, “disseminated cysticercosis”. The parenchymal cysts were not associated with cerebral edema. The patients with disseminated cysticercosis manifested with neuropsychiatric syndromes and dementia in the absence of features of intracranial hypertension. This disseminated form, as well as cysticercal encephalitis, constitute one end of the spectrum of neurocysticercosis, while the limited solitary lesions occur at the other end of the spectrum.

At this stage it may be emphasized that the solitary parenchymal cysticercus cyst is not found in India alone, but is known to occur in other geographic locations as well. Mitchell and Crawford, reported a series of 52 paediatric patients with cerebral cysticercosis from Los Angeles. Sixty four percent of their patients had a single lesion on CT. The authors referred to these lesions as “inflamed single intraparenchymal cysts”. These lesions appear identical to the SSECT lesions observed in Indian patients with epilepsy.

An association of neurocysticercosis with Japanese B encephalitis appears to be unique to South Asia. Japanese B encephalitis is endemic in East and South India. Shankar et al., in an autopsy study of patients who died because of Japanese B encephalitis, found neurocysticercosis lesions in 35 percent of the brains. While it is known that cysticercosis can be detected incidentally at autopsy, the reported incidence of neurocysticercosis in autopsy studies of brain during epidemic
Fig 1. Plain (a) and contrast enhanced (b) CT in a patient with focal seizures showing a ring enhancing lesion with surrounding edema. There is no midline shift. Repeat plain (c) and contrast enhanced (d) CT scan was done 14 weeks later. The ring lesion had disappeared leaving behind a spec of calcification and the edema has resolved. Resolution occurred without any specific therapy.

Japanese B encephalitis appears to be unduly high. The observation has led on to the assumption that cysticercosis somehow predisposes the host to acquire Japanese B encephalitis. An ante-mortem association of Japanese B encephalitis and neurocysticercosis has also been described. The association is important because both neurological disorders are common in South Asia. Cysticercal encephalitis would constitute an important clinical differential diagnosis of such an association.
**Immunological Studies:** Several serologic tests including the indirect haemagglutination assay, plate ELISA, dot ELISA and EITB, are available for the immuno-diagnosis of cysticercosis\textsuperscript{16,17,28,51}. For a detailed account of these tests, the reader is referred to a review by Flisser et al\textsuperscript{16}. Any present day serological evaluation of cysticercosis should be based on EITB assay\textsuperscript{51}. The latter has been assessed in epidemiological surveys in the American continent\textsuperscript{13,39,42}. Experience with the EITB assay in the Indian subcontinent is rather limited and the need for performing serosurveys in the part of the world has already been stressed.

The CSF is the most appropriate biological fluid for diagnosis of neurocysticercosis. Positive CSF indirect haemagglutination assays correlate with meningeal involvement. Mc Cormick et al\textsuperscript{28} reported positive CSF titers in 84% of their patients with meningitis and in only 42% of patients without evidence of meningeal involvement. Since cysticercal meningitis is uncommon in India, the number of positive CSF titers is comparatively lower in Indian patients\textsuperscript{12,51}.

**Modalities of transmission:** In the subsequent section, an attempt is made to evaluate factors responsible for different presentations of neurocysticercosis described in the Indian and South and Central American series. Factors which influence clinical manifestations of neurocysticercosis may be categorised into host related and parasite related factors. Age, sex and immune status are important host related factors\textsuperscript{34,37}. The occurrence of cysticercal encephalitis, a particularly severe form of infestation in female patients, has led several authors to postulate that sex and immune status are responsible for the clinically heterogeneous manifestations of neurocysticercosis\textsuperscript{37}. It would be interesting to evaluate immunological status of persons with limited cysticercus lesions versus multilesional neurocysticercosis. However, such studies are likely to be biased because of the effect of parasitemia on immune functions\textsuperscript{32}. Therefore tests of immunological function, which are independent of parasite numbers should be used. A preliminary evaluation could not find any difference in the mean 3,4-thymidine uptake after T cell stimulation with phytohaemagglutinin, between patients of multilesional neurocysticercosis and presumed solitary neurocysticercosis\textsuperscript{50}.

In the opinion of the author, important factors, which influence the cyst load are the food and meat preferences of the host individuals. As mentioned earlier, a good proportion of Indians are vegetarian and do not consume pork. The occurrence of cysticercosis in Indian subjects who are vegetarians has not been fully explained. It has been suggested that consumption of raw vegetables contaminated by taeniid eggs can cause cysticercosis in vegetarians. A good proportion of villagers and slum dwellers in India defecate in the fields because of the inavailability of sanitary methods of faecal disposal. This practice may lead to contamination of vegetables grown in the fields. Consumption of improperly washed raw vegetables has been implicated in the transmission of cysticercosis. However, preliminary studies have failed to demonstrate the presence of cestode eggs in samples of vegetables and field soil (Singh and Juyal, personal communication). There is no firm evidence or suggestion that contamination of raw vegetables is actually involved in transmission of cysticercosis. Possibly a more significant method of transmission is through food handlers, who themselves are taenia carriers. Unhygienic practices of these food handlers can lead to the contamination of food prepared by them with taeniid eggs. Persons consuming such food are at risk of developing cysticercosis. Since such persons are not themselves taeniid carriers, they have a limited exposure to cestode ova and are hence likely to acquire only a limited cyst load. The argument follows that single cysticercus lesions generally develop in persons who do not themselves consume contaminated pork and do not have intestinal taeniosis. These lesions are likely to be acquired through infected food handlers.

Consumption of pork infested with cysticercus larvae causes intestinal taeniosis. Recurrent autoinfection in taeniid carriers causes multiple cysticercosis. Therefore multilesional cysticercosis occurs in subjects who consume pork and have *Taenia solium* infestation. The cyst load in a given population appears to be linked to the frequency of consumption of contaminated pork. Since pork
ingestion is frequent and the infestation is very high in South Central America, the proportion of multilesional cases is high in Hispanics.

**Economic issues:** The large scale Hispanic immigration and the proximity of Mexico and other Latin American countries has led on to unprecedented research efforts into various aspects of cysticercosis, in the United States. Considerable funding is available for studying epidemiological and immunological attributes of cysticercosis in American countries. Developed countries should also focus on India for the establishment of collaborative research, because clinical patterns in the non immigrant local population may actually resemble patterns found in India.

**REFERENCES**

55. Wadia RS, Makhale CN, Kelkar AV, Grant KB. Focal epilepsy in India with special reference to lesions showing ring or disc like enhancement on contrast computed tomography. Neurol Neurosurg Psychiatry 1987;50:1298-1301.