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Diagnosis of cysticercosis in endemic regions

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Abstract

Taenia solium cysticercosis is a frequent cause of neurological disease in developing countries. Specific diagnosis of cysticercosis is difficult. We obtained serum and/or CSF samples from 204 consecutive patients admitted to a neurological ward in Lima, Peru, and looked for antibodies specific for *T solium* with the enzyme-linked immunoelectrotransfer blot (EITB) assay. 21 (12%) of 173 serum samples from these patients were EITB-positive. In contrast only 2 (1·5%) of 135 patients attending a public endoscopy clinic and 1 (1%) of 88 patients attending a private endoscopy clinic were seropositive. 1 (1%) of 98 pregnant women living in a Lima shanty town was EITB-positive. 15 (58%) of 26 neurology patients diagnosed clinically as having cysticercosis were seronegative. Routine screening by EITB of all patients with neurological symptoms from areas of endemic cysticercosis would avoid misdiagnosis of this common and treatable disease.

Introduction

The life cycle of the cestode *Taenia solium* involves an intermediate host, normally the pig, for the cystic form of the parasite and a definitive host, normally man, for the adult form or tapeworm. However, persons infected by *T solium* eggs can also serve as hosts for the cystic form, which frequently attacks the central nervous system. Cysts may also be found in the subcutaneous tissue, muscle, and eye,[1,2] and, more rarely, in other parts of the body.[3,4] *T solium* cysticercosis is common in countries where free-ranging pigs are raised.[5–7]

Many factors affect the clinical manifestations of the disease, including the number, size, location, and form of the parasites, and the immune response of the host. The interaction of these factors produces a spectrum of neurologic symptoms.[1–5,8–12]

Correct diagnosis of cysticercosis is important since most patients respond to treatment with albendazole or praziquantel. However, diagnosis is difficult. The disease is usually

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diagnosed on the basis of clinical symptoms, including the occasional presence of subcutaneous nodules, and confirmed by computed tomography (CT) or nuclear magnetic resonance imaging (MRI); but CT and MRI are rarely available in endemic areas. Until recently serological tests, including the enzyme-linked immunosorbent assay (ELISA), were not sensitive and specific enough to confirm the diagnosis, especially in areas where other cestode infections are endemic.[12–14]

Development of the enzyme-linked immuno-electrotransfer blot (EITB) assay,[15] has provided a precise method of diagnosing *T solium* infection in neurological patients. Here we report use of this new immunological test to detect antibodies to *T solium* in patients admitted to an acute-care neurological ward in Lima, Peru.

Patients and methods

Patients

All new patients (n = 231) admitted to the male neurological ward at the Instituto Nacional de Ciencias Neurológicas (INCN) in Lima, Peru, between September, 1988, and June, 1989, were entered into the study. The INCN is the neurological reference centre for Peru, serving mainly lower and middle class sections of the population. Serum samples for EITB assay were taken from all patients at admission, and when cerebrospinal fluid (CSF) was obtained for clinical reasons a sample was set aside for assay. Informed consent was obtained from all patients. The study was approved by the ethical review boards of the Universidad Peruana Cayetano Heredia, Lima, and the Johns Hopkins University, Baltimore, USA.

Clinical histories and results of physical examinations were reviewed, and, when available, the diagnosis obtained after CT scan was recorded. CT scans are done infrequently in Peru because of their cost; MRI is not available in Peru. After the initial clinical diagnosis had been recorded, EITB results were made available to doctors managing the patients.

Patients may be free of symptoms of cysticercosis but seropositive. To determine the proportion of seropositive patients without neurological disease, we used EITB to assay serum samples from two groups of patients attending endoscopy clinics for treatment of gastrointestinal symptoms. One group were 135 poor or lower-middle-class patients who visited a public endoscopy clinic (34 men, 101 women; mean [SD] age 42 [17·9] years, range 18–94), and the other group were 88 middle or upper class patients attending a private endoscopy clinic (48 men, 40 women; mean age 48 [16·1] years, range 16–82). To determine the rate of symptom-free cysticercosis in individuals born or living in Lima, we surveyed the sera of 98 pregnant women (mean age 28 [5·81], range 17–43) from a shanty town in Lima.

EITB assay

The EITB assay for antibodies specific for *T solium* was done as described previously.[15] Briefly, seven lentil-lectin purified *T solium* glycoprotein antigens are used in an immunoblot to detect specific antibodies in serum or CSF. Antibody reactions against these glycoproteins are visualised with H_2O_2/diaminobenzidine substrate, and reactions to one or more glycoprotein are considered a positive result. The assay was repeated when results were ambiguous. Tests were done at the Laboratory of Parasitology of the Universidad Peruana Cayetano Heredia, and duplicate specimens were sent to the Centers for Disease Control, Atlanta, USA, for quality control.

Definitions

Clinical diagnosis—The clinical diagnosis of cysticercosis was not standardised but rather reflected the consensus opinion of the attending neurologists. In general, patients admitted to the neurological ward who had lived in areas of endemic cysticercosis and had late-onset seizures or raised intracranial pressure were diagnosed as having cysticercosis.

CT scan diagnosis—CT scans are indicated in all patients with chronic or focal neurological disease. However, in Peru many patients cannot afford a CT examination; thus, most scans were done based on medical and economic criteria. The following radiological criteria, any one of which was compatible with a diagnosis of neurocysticercosis, were used: one or more cystic images, two or more calcifications, and/or one or more nodules visualised after injection of contrast medium. The last criterion is compatible with a diagnosis of either tuberculosis or cysticercosis.

Results

Of the 231 patients admitted to the neurological ward, 204 (88%) provided serum (n = 173, 75%) and/or spinal fluid (n = 166, 72%) for testing. 21 (12%) serum samples and 18 (11%) CSF samples were EITB-positive. Matched CSF and serum samples were obtained from 135 patients—19 (14%) of these serum samples and 17 (13%) CSF samples were EITB-positive; thus, 2 CSF samples were negative when the matching serum sample was positive. No serum sample was negative when the matching CSF sample was positive. There were no differences in age or clinical characteristics between EITB-positive and EITB-negative patients (table I). Although the length of hospital stay was longer for seropositive patients than for seronegative patients, this difference was not significant. The mean [SD] age of the 27 patients who did not provide samples was similar to that of the 204 individuals who were sampled (44 [19] years, range 19–79 *vs* 42 [18], range 14–88). However, the unsampled patients had a significantly shorter mean [SD] length of hospital stay (8 [8·8] days *vs* 31 [28·4]; $p < 0·01$, Mann-Whitney test).

Of the 204 patients who provided samples for testing, 26 had a clinical diagnosis of cysticercosis and 11 (42%) of these 26 patients were seropositive. 10(6%) of the 178 patients not given a clinical diagnosis of cysticercosis were seropositive (table I). Of the 10 seropositive patients not initially diagnosed as having cysticercosis, 1 was a *T solium* adult worm carrier, 1 had previous surgery for cerebral cysticercosis (not recorded on the admission history), 3 had cerebral CT scans showing multiple cystic images, 1 had a CT image of an expanding temporal process, and another had severe hydrocephalus with non-specific pachymeningitis at necropsy. The CT scans were done before results of EITB assay were known. The 3 remaining patients were admitted for diverse clinical signs: 1 for seizures, another for trauma but with a history of occipital lobe seizures, and the third for a stroke. These 3 patients did not have CT scans or parasitological stool examinations.

Clinical findings in the 56 patients admitted to the neurological ward who had a cerebral CT scan are shown in table II. The EITB-positive patient with a normal CT scan had an ocular cysticercus and an adult tapeworm. 6 of the 15 seronegative patients clinically diagnosed as having cysticercosis had a cerebral CT scan; 3 scans were diagnosed as showing cysticercosis (calcifications as the only CT scan finding), 1 showed a neoplasia, and 2 scans were normal.

2 (1·5%) of the 135 patients attending a public endoscopy clinic were EITB-positive. 1 of the patients was symptom-free and no history was available for the other. 1 (1 %) of 88 patients seen at the private endoscopy clinic was EITB-positive. This individual was without neurological symptoms and had a normal CT scan. Only 1 (1%) of the 98 pregnant women

was EITB-positive and she was also without neurological symptoms. All seropositive subjects in the comparison groups were born in rural pig-raising areas.

Discussion

In developing countries, investigation of patients with neurological symptoms is limited by economic factors. Routine analyses are reduced to those strictly necessary and special radiological studies, such as CT scans, are often available only to privileged members of the population. In Peru, Mexico, and Brazil, cysticercosis is found during 6–7% of necropsies done at neurological centres.[16–18] Patients suspected of having cysticercosis occupy 10–15% of the beds in neurological wards (M. Martinez, personal communication). Besides being common, hospital admissions for cysticercosis can be longer than for most other neurological diseases.[16] The combination of high prevalence and prolonged hospital admissions gives rise to high health–care costs.

Cysticercosis is frequently misdiagnosed clinically. The EITB technique is a sensitive and specific assay for the diagnosis of cysticercosis that is as sensitive in serum as it is in CSF.[15] We detected a high prevalence of cysticercosis (11 %) by EITB in patients admitted to a neurological ward. Cysticercosis was not the initial diagnosis in most of these patients. CT scan, although highly specific, was relatively insensitive compared with EITB for diagnosing cysticercosis. In addition, most patients diagnosed clinically as having cysticercosis did not have serological evidence of this infection. None of the 6 seronegative patients who had a clinical diagnosis of cysticercosis and a CT scan had any radiological evidence of active cysticercosis lesions. 3 of these 6 patients had multiple calcifications; thus, we cannot exclude the possibility that these patients converted from seropositive to seronegative after their lesions calcified.

In our laboratory, the EITB assay has 95% sensitivity and 100% specificity.[20] The EITB assay will give positive results with patients who are infected with either the tapeworm or the cystic form. In a region of endemic cysticercosis, many seropositive individuals may be symptom-free if they are infected with occult cysts or intestinal tapeworms. To control for silent infection, we examined patients from different social classes who came to hospital for endoscopy. Prevalence (positive EITB) was seven times higher in neurological patients than in those coming for endoscopy, suggesting strongly that seropositivity and neurological symptoms are linked. Additionally, only 1 of 14 neurology patients with normal CT scans was EITB-positive. It appears that most EITB-positive patients admitted to the neurological ward had symptomatic neurocysticercosis.

Patients who did not provide serum of CSF samples had a shorter hospital stay than those who did. This unsampled group may have had a lower proportion of EITB-positive cases. However, even if all 27 unsampled patients were EITB-negative, and we had included them in the analysis, the EITB-positive rate would still be 9·5%.

None of our patients with neurological symptoms had a positive serological test for syphilis or human immunodeficiency virus. Although less than 0·5% of neurological patients admitted to the INCN have positive syphilis serology according to hospital records, syphilis screening is done routinely. Cysticercosis is 10–20 times more frequent than syphilis in Peru, but routine screening is not done. We recommend that in endemic areas all patients with neurological symptoms be screened routinely for cysticercosis by EITB to avoid misdiagnosis of this treatable disease.

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TABLE I

COMPARISON OF SEROPOSITIVE AND SERONEGATIVE PATIENTS WITH NEUROLOGICAL SYMPTOMS

—	Sero-positive (n = 21)	Sero-negative (n = 183)	Significance
Mean (SD) age (yr)	44 (17·9)	42 (20·8)	NS (Student's *t* test)
Mean (SD) hospital stay (day)	45 (43·4)	29 (25·8)	NS (Mann-Whitney test)
No (%) with headache	11 (52)	83 (45)	NS (χ^2 test)
No (%) with seizures	10 (48)	54 (30)	NS (χ^2 test)
No (%) with motor deficit	6 (29)	82 (45)	NS (χ^2 test)
No (%) with cranial nerve compromise	4 (19)	34 (19)	NS (Fisher's test)
No (%) with clinical diagnosis of cysticercosis	11 (52)	15 (8)	--
No (%) without clinical diagnosis of cysticercosis	10 (48)	168 (92)	--

NS = not significant.

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TABLE II

RESULTS OF EITB IN PATIENTS WHO HAD A CEREBRAL CT SCAN

CT finding	EITB-positive	EITB-negative
Normal (n = 14)	1	13
Cysticercosis (n = 14)	11	3
Vascular disease (n = 14)	3	11
Neoplasia (n = 7)	0	7
Other infectious diseases (n = 5)	0	5
Hydrocephalus (n = 2)	1	1
Total (n = 56)	16	40