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DISCREPANCIES BETWEEN CEREBRAL COMPUTED TOMOGRAPHY AND WESTERN BLOT IN THE DIAGNOSIS OF NEUROCYSTICERCOSIS

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Abstract. Serum samples from sequential patients who underwent cerebral computed axial tomography (CT) scan in a Peruvian radiologic clinic were tested by the highly sensitive and specific enzyme-linked immunoelectrotransfer blot (EITB) test to detect antibodies to *Taenia solium*. The results of the EITB test were compared with those obtained by CT scan for the diagnosis of neurocysticercosis. Of the 383 patients sampled, 32 (8%) were seropositive. The results of CT and EITB were frequently discrepant. When compared with the EITB assay, the CT scan was 44% sensitive and 95% specific. The sensitivity of CT increased to 63% if less specific images (single calcifications, granulomas, or hydrocephalus) were included. The CT scan for diagnosis of cysticercosis can best be used in conjunction with a reliable serologic test such as the EITB.

Taenia solium cysticercosis is an important parasitic disease affecting the human central nervous system (CNS).[1,2] Cysticercosis is common in those developing countries where free-ranging pigs are raised.[3] The life cycle of this cestode requires an intermediate host, normally the pig, for the cystic form of the parasite and a definitive host, humans, for the adult tapeworm.[4] However, humans infected by *Taenia* eggs serve as the intermediate host and develop the cystic form. Besides the CNS, cysts may also be found in the subcutaneous tissue, muscle, and eye,[5,6] and more rarely in other parts of the body.[7]

Many factors affect the clinical presentation of cysticercosis, including the number, size, location, and form of the cysts and the immune response of the host. The interaction of these variables results in a wide spectrum of neurologic symptoms.[1,2,5,7]

Cerebral computed axial tomography (CT) has been the method of choice for the diagnosis of neurocysticercosis.[1,5] However, CT images are not pathognomonic for this disease and apparently positive tests findings can be caused by a variety of other conditions.[8-10] The CT scan has been claimed to have a sensitivity and specificity of about 95%,[1,11] but controlled studies are not available. Approximately 25% of cysticercosis cases occur in the racemose form, in which the cysts are located at the base of the brain. Such basal cysts appear on CT only as hydrocephalus or deformation of the basal cisterns.[4,12] Cysticerci also present as granulomas or nodular forms, which often are indistinguishable from other granulomatous conditions such as tuberculosis.[8,13,14]

Evaluation of the sensitivity and specificity of the CT scan for the diagnosis of cysticercosis requires a standard for comparison. Until recently, the only standards available for testing the accuracy of CT were the results obtained by postmortem examination or neurosurgical exploration.[15] The recently developed enzyme-linked

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immunoelectrotransfer blot (EITB, Western Blot) assay[16,17] provides a precise method of diagnosing *T. solium* infection. In this study, we used the EITB assay as a standard to determine the sensitivity and specificity of cerebral CT in patients admitted to a radiologic center for diagnosis of neurologic symptoms.

MATERIALS AND METHODS

The study was conducted in a private radiology center in Lima, Peru. After informed consent was obtained, blood samples were collected for EITB from patients admitted during normal working hours for cerebral CT examination during two separate periods (September 16–October 12, 1988 and February 6–May 2, 1989). Sampling was often not possible during clinic off hours and episodes of labor unrest. Normal working hours for the clinic are between 9:00 AM and 1:00 PM, and from 4:00 PM to 8:00 PM. Occasionally, patients are admitted outside of normal working hours on an emergency basis. These emergency patients are not sampled. In addition, on a few occasions, our study nurse was unable to visit the clinic; therefore, no sample was taken during these rare occasions. The study was approved by the ethical review boards of both the Universidad Peruana Cayetano Heredia and the Johns Hopkins University.

Axial computed tomography scans

All scans were performed on an Exel 2002 scanner (Elscint, Haifa, Israel) with a 140–480-mm scan circle and a 5.3–5.8 sec scan time. Two image series were made using 10-mm slices. Patients were examined before and after contrast injection (iodamide metylglucamate, Uromiron®, 1 ml/kg; Schering G.A., Berlin, Germany). The scans were read by a neuroradiologist (GH) who did not know the results of the EITB assay. The CT scans of patients who were diagnosed as having cysticercosis but had a negative EITB result were read blindly by a second neuroradiologist.

Axial computed tomography scan diagnosis of cysticercosis

Radiologic criteria for the diagnosis of neurocysticercosis by CT are not uniform.[11,18,19] We used the following criteria, modified from a previous study:[20] 1) one or more cystic images and/or 2) two or more compatible calcifications. Calcifications were considered compatible if they were not located in zones of physiological calcifications,[21] were annular or rounded, and were less than 10 mm in diameter.

Other diagnosis

The neuroradiologist's reports were classified as follows: 1) normal CT scan, 2) cysticercosis, 3) vascular disease, and 4) neoplasia. We also noted the presence of 1) cystic images, 2) abnormal calcifications, 3) granulomatous images, 4) hydrocephalus, and 5) cortical or subcortical atrophy.

Enzyme-linked immunoelectrotransfer blot assay

The EITB assay for *T. solium*–specific antibodies was performed as previously described.[16] Briefly, seven lentil-lectin purified *T. solium* glycoprotein antigens are used in an immunoblot format to detect infection-specific antibodies in serum or cerebrospinal fluid (CSF) samples. The assay was performed in the Accutran system (Schleicher & Schuell, Keene, NH). Antibody reactions against these glycoproteins in serum and/or CSF were visualized with the H_2O_2/diaminobenzidine (DAB) substrate system.[22] An antibody reaction to one or more glycoprotein bands was designated a positive result. Equivocable assays were repeated. Assays were performed at the Laboratory of Parasitology of the Universidad Peruana Cayetano Heredia, and duplicate specimens were sent to the Centers for Disease Control and Prevention (CDC, Atlanta, GA) for quality control.

RESULTS

Sample characteristics

Three hundred eighty-three (63%) of 606 patients classified underwent cerebral CT had a blood sample taken for the EITB. Comparison of the sampled patients with those not sampled showed that the two groups were similar in age, sex ratio, and the proportion of patients diagnosed as having cysticercosis or neoplasia (Table 1). However, the sampled group had significantly ($P < 0.001$) more normal CT scans, probably because the majority of these patients

TABLE 1

Comparison of sampled and unsampled patients undergoing cerebral computed tomography (CT) scan examination

	Sampled (n = 383)	Unsampled (n = 223)	P*
Age, years (mean ± SD)	40 ± 22	39 ± 28	NS
No. (%) males	223 (58)	122 (55)	NS
CT diagnosis, no. (%)†			
Normal CT scan	114 (30)	31 (14)	<0.001
Trauma	32 (8)	41 (18)	<0.001
Vascular disease	86 (22)	74 (33)	<0.01
Neoplasia	35 (9)	17 (8)	NS
Cysticercosis	30 (8)	12 (5)	NS
Others	110 (29)	74 (33)	NS
CT characteristics, no. (%)			
Hydrocephalus	30 (8)	28 (13)	NS
Atrophy	72 (19)	47 (21)	NS
Calcifications	38 (10)	13 (6)	NS

* *P* was determined by the chi-square test. The difference in mean age was tested by student's *t*-test. NS = not significant.
† Some patients had more than one pathology in the same CT scan.

came during working hours. In contrast, patients with acute trauma or vascular accidents often were not sampled because they came to the clinic at irregular hours when sampling did not occur (Table 1).

Results of EITB assay

Of the 383 patients sampled, 32 (8%) had EITB assay results positive for antibodies to *T. solium*. No differences in age or sex distribution were found in EITB-positive versus EITB-negative patients (Table 2).

Results of the EITB and CT

Thirty patients were diagnosed as having cysticercosis by EITB and 32 by CT scan. The results obtained in the CT scan and the EITB assay were frequently discrepant. More than 50% of the cases diagnosed as cysticercosis by the radiologist were EITB- negative (Table 2). Compared with the EITB, the CT scan was only 44% sensitive, detecting 14 of 32 EITB-positive patients. However, CT and EITB diagnosis of cysticercosis were significantly associated when the whole study population is examined. No patient with CT-diagnosed neoplasia had positive EITB

TABLE 2

Characteristics of enzyme-linked immunoelectrotransfer blot (EITB)-positive and EITB-negative patients and comparison of results with computed tomography (CT) scan diagnosis

	EITB+ (n = 32)	*EITB−* (n = 351)	P*
Age, years (mean ± SD)	45 ± 20	40 ± 22	NS
Age, years (range)	9–82	0–85	
No. (%) males	20 (63)	202 (58)	NS
CT diagnosis, no. (%)†			
Normal CT scan	5 (16)	109 (31)	NS
Trauma	2 (6)	30 (9)	NS
Vascular disease	5 (16)	81 (23)	NS
Neoplasia	0 (0)	35 (10)	NS
Cysticercosis	14 (44)	16 (5)	<0.001
Others†	8 (25)	102 (29)	NS

* *P* was determined by either Fisher's exact test or chi-square test. The difference in mean age was tested by Student's *t*-test. NS = not significant.
† Some patients had more than one pathology in the same CT scan.

results, and patients with normal scans tended to have a lower percent of EITB seropositivity (Table 2). The overall specificity for CT, derived from dividing all CT-negative patients (335) by all EITB-negative patients (351), was high (95%).

The 18 patients with positive EITB but negative CT scan results had the following tomographic characteristics: five appeared normal, four had atrophy, three had a single calcification, two had hydrocephalus, two had subdural hematomas, one had a surgical sequel for trauma, and one had a granuloma.

There were 16 patients whose results were EITB negative but CT scan positive. In the initial CT report, six of them were diagnosed with inactive cysticercosis (only calcifications), and the remaining 10 had at least one cystic image (active cysticercosis), in five cases coexisting with calcifications. Fourteen of those 16 scans were reread by another neuroradiologist (EJC), also blinded to the EITB. Five were reported as not having cysticercosis (three as normal) and eight as having inactive cysticercosis. Only one of the 10 patients diagnosed as having active cysticercosis by the first reader was considered active by the second (Table 3).

Subsequent to this study, eight of these 16 patients had at least one additional sample examined by EITB, including six with CSF samples. All samples were negative.

TABLE 3

Reproducibility of neuroradiologic diagnosis in a group of 14 computed tomography–positive enzyme-linked immunoelectrotransfer blot (EITB)–negative patients

	Active cysticercosis	Inactive cysticercosis	No cysticercosis
Neuroradiologist 1	10	4	–*
Neuroradiologist 2	1	8	5

* Reports on 14 patients who were diagnosed as having cysticercosis by the first radiologist and who had a negative EITB result. Scans of two patients were not recovered from the archives.

DISCUSSION

In this study, we used the highly sensitive and specific EITB assay for the detection of antibodies to *T. solium* infection to assess the accuracy of the CT scan for the diagnosis of cysticercosis. Eight percent of the patients scanned had a positive EITB test result, providing further evidence that cysticercosis is endemic in Peru.[20, 23]

When measured by the EITB test, the sensitivity of the CT scan was only 44%. If less specific images such as hydrocephalus, granulomas, and single calcifications were considered, the overall sensitivity was 63%. Because the EITB can only determine whether a patient is infected with *T. solium* but not whether the infection is located in the CNS, the EITB will underestimate the sensitivity of the CT scan. Thus, discordance between a negative CT and a positive serodiagnosis is not necessarily due to misdiagnosis but may represent the presence of an adult worm or extracerebral cysts. Another possibility is that some patients have the racemose form of the disease, in which cysts are located at the base of the brain. Basally located cysts often do not show up on a CT scan except as hydrocephalus.[1] Magnetic resonance Imaging (MRI) may detect these lesions as well as small intraparenchymal lesions missed on a CT scan;[24, 25] however, MRI scanners are rarely available in endemic areas.

Certainly in patients with multiple calcifications, which are end-stage lesions, the active disease that caused the calcifications cannot be known. Moreover, EITB-negative patients with calcified scars or hydrocephalus may have had active cysticercosis in the past but their immunity may have waned. It is still not known how long antibody persists in patients whose cysts have resolved. Regrettably, the patients in this study were referrals to a private radiology center for CT examinations only. Results of the EITB and CT were reported to their respective primary physicians, who provided appropriate treatment. Within the constraints of the present study, therefore, we were not able to provide direct treatment or follow-up for these patients.

The specificity of CT is high (95%) when all patients are included. When positive CT results were compared with EITB assay results, the specificity of CT was much poorer. More than 50% of the patients diagnosed as having cysticercosis by CT were EITB negative. There are several possible reasons for this. First, although the specificity of the EITB test has not been questioned, its sensitivity may vary with specific lesions.[16, 20] A recent report states that single intraparenchymal lesions are often associated with a negative EITB test result.[26] Unfortunately, the population of this study was self-selected, and thus true sensitivity cannot be calculated. Second, different readers may have a wide variance

in CT interpretation,[27] especially for small lesions. Finally, overdiagnosis probably occurs because of multiple other causes, including fungal infections, chronic abscesses, tuberculosis, and cystic neoplasms, for images seen on scans reported as cysticercosis.

In an endemic zone, cerebral CT was not read as cysticercosis in more than one-third of the EITB-positive neurologic patients. The diagnosis of this disease will be markedly improved if CT is used in conjunction with an accurate immunologic assay such as the EITB.

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