CYSTICERCOSIS IN CHRONIC PSYCHIATRIC INPATIENTS FROM A VENEZUELAN COMMUNITY

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Abstract. Cysticercosis due to *Taenia solium* infection is endemic in developing countries of the Americas, Asia, and Africa. This study was designed to establish the prevalence of cysticercosis in 158 inpatients of a psychiatric institution in the state of Táchira (Venezuela) and in 127 healthy control subjects. Positive blood tests for cysticercosis by Western blotting were recorded in 18.35% of the patients and in 1.57% of the controls. Individuals with mental retardation were found to carry an increased risk of cysticercosis (RR: 2.92; 1.22 < 2.92 > 7.0; *P* < 0.05) compared with patients with other psychiatric disorders. Taeniaisiasis was not demonstrated in the patient group, although a high incidence of infection by other helminths (95.1%) was detected. The high prevalence of cysticercosis in the psychiatric inpatient group, compared with healthy individuals, and the lack of a differential diagnosis of neurocysticercosis suggest cerebral cysticercosis in a large proportion of these patients. Cysticercosis could be the origin of the psychiatric disorders of these patients and may also be due to contact with the parasite in an environment with poor hygiene conditions and a deficient health care system.

INTRODUCTION

Taeniaisiasis and cysticercosis are significant health problems related to underdevelopment. These tapeworm infections appear in countries where free-range pigs are raised in poor hygiene conditions and health education in the population at large is inadequate. Although taeniasis tends to be asymptomatic, human cysticercosis is a complex disease with a varying clinical presentation. Its main manifestations depend on the parasite status (number, location, and stage) and the host-immune response. The most significant clinical signs appear when metacestode invasion of the central nervous system (CNS) occurs, which causes a chronic and sometimes fatal disease called neurocysticercosis (NCC). NCC is the most common CNS parasite infection and an important health problem in developing countries in the Americas, Asia, and Africa. In industrialized countries, a significant number of new cases have been reported as a result of increased immigration from endemic areas.

NCC presents with a varying clinical picture, although the wide range of signs and symptoms produced can be grouped into three main classes: convulsions, intracranial hypertension, and psychiatric disorders. Diagnosis is difficult and requires several procedures. A comprehensive clinical assessment together with suitable interpretation of neuroimaging and immunologic tests are essential for diagnosis and proper management. In endemic regions, NCC is checked for in the differential diagnosis of most neurologic disorders. NCC is suspected in patients who present with convulsions, hydrocephalus, and cystic brain lesions even in nonendemic areas. Despite this, NCC is rarely considered when psychiatric disorders are evaluated, and NCC-related psychiatric manifestations have scarcely been described. Psychiatric symptoms are common in patients with NCC, and mental disease could be the consequence of the deteriorating organic illness. Moreover, mentally disabled patients may show an increased risk of neurocysticercosis due to infection by contact with feces resulting from poor hygiene and unsatisfactory medical care.

In this study, we describe the prevalence of taeniasis and cysticercosis in chronic inpatients from a psychiatric institution in Venezuela.

MATERIALS AND METHODS

Patients and control subjects. The study population was composed of 158 of the 207 inpatients of the Psychiatric Institution “Dr. Raul Castillo” in the state of Táchira in Venezuela. All tests were performed with patient consent. We also obtained written informed consent from each patient’s legal guardian, as well as from the institution’s Board of Physicians. Relevant demographic and medical data were obtained from the patients’ clinical records. Psychiatric diagnosis was made according to DSM-III-R diagnostic criteria and backed by the psychiatric history of the patient. Blood samples were taken from all patients for enzyme-linked immunosorbent assay (ELISA) and enzyme-linked immunoelectrotransfer blot (EITB) assays. Only 61 provided stool samples, the remaining patients refusing to collaborate in the parasite analysis. Blood and stool samples were also taken from 127 selected healthy subjects with no prior history of psychiatric disorders and who were well matched with the patients in terms of demographic characteristics (sex, age, socioeconomic status, and place of origin). All participants provided written informed consent before enrollment. The study was approved by the Institutional Review Board of the University of Los Andes and the Ethics Committee of the National Foundation of Science, Technology, and Innovation (FONACIT) of the Ministry of Science and Technology, Venezuela.

Immunodiagnosis. Antibodies against *Taenia solium* antigens were detected by ELISA. Antigen extracts were obtained from *Taenia crassiceps* cysticerci (ORF strain) as previously described by other authors. Phenylmethylsulfonylfluoride (Sigma Chemical Co., St. Louis, MO) was added...
to the extracts until a final concentration of 0.4 mM was attained and preparations were stored at −70°C. 96-Well flat-bottom polystyrene plates (Costar Corporation, Cambridge, MA) were incubated with *T. crassiceps* extracts (1 μg/mL in citrate buffer [0.2 M], pH 5.0) at 4°C overnight. Skimmed milk (2%) in saline solution containing 0.05% Tween 20 was used as a blocking agent for 2 hours at 37°C. Serum (diluted 1:250), conjugate (peroxidase-labeled goat anti-human immunoglobulin G [whole molecule; Sigma Chemical Co.]), and chromogen substrate (ortho-phenylenediamine [1 g/L] and H₂O₂ [1 mL/L]) were used in the ELISA assay. All incubations steps were carried out at 37°C for 1 hour except for those conducted with the substrate (15 minutes). The reaction was stopped with 0.5 N H₂SO₄ and the plates read with a plate spectrophotometer (Organo Teknika, Durham, NC). The serum sample was recorded as positive when a diluted sample (1:250) had a specific optical density (OD), read at 492 nm, of 3 standard deviations (SD) above the mean value of the negative control samples.

*Taenia solium* metacestode-specific IgG antibodies were detected using a Western blot kit for cysticercosis (Immunetics Inc., Boston, MA).

This commercial EITB assay is based on the method described by Tsang and colleagues.²⁷ Briefly, seven lentil-lectin purified glycoprotein antigens are used in an immunoblot to detect specific antibodies in serum. Antibody reactions against these glycoproteins were visualized using H₂O₂/diaminobenzidine substrate. Reactivity for one or more glycoproteins was considered a positive result.

**Stool analysis.** Stool specimens were collected into disposable plastic cups and a portion of each sample was then placed in a tube containing 10% formalin. These specimens were concentrated using the Ritchie formalin ether sedimentation concentration procedure and two slides were made from the resulting pellet.²⁶ Ova from *Taenia* spp. and other helminths were identified by microscopic examination under 10× and 40× power.

**Statistical analysis.** Descriptive statistics were used to summarize information and baseline characteristics for each subject. Proportions were compared by χ² or Fisher’s exact tests (for cross-tabulations with an expected value of ≥5 in any cell). Tests were considered significant if two-tailed *P* values were <0.05. Relative risks (RR) and 95% confidence intervals (CI) were also calculated. All statistical analyses were performed using SPSS (version 7.5; SPSS, Chicago, IL) and Epi-Info 6 software.

**RESULTS**

**Demographic study.** The demographic characteristics of the patients and control subjects are shown in Figure 1. Most of the 158 patients enrolled came from rural areas (*P* < 0.05) (Figure 1c). Socioeconomic status analyzed by means of Graf-far’s method for Venezuela revealed a high level of poverty.²⁹ The majority of patients were from levels having the lowest standard of living, levels IV and V, respectively; and most (60.5%) were classified as critical poverty status level V (Figure 1d).

![Figure 1. Main demographic characteristics of the patients and controls: (a) gender, (b) age-stratified distribution, (c) place of origin, and (d) socioeconomic status.](image-url)
Immunologic evaluation. Figure 2 provides the ELISA and EITB results for the psychiatric patients and controls. Of the 158 patient blood samples tested for *Taenia solium* antigenic antibodies by ELISA, a positive result was obtained in 51 (32.28%). There were no gender-related differences between ELISA-positive and ELISA-negative patients. Similar findings were also observed when the patients were stratified according to their socio-economic level and place of origin (rural versus urban). Seroprevalences determined by ELISA differed significantly between the psychiatric patients (32.28%; 51 of 158) and controls (6.3%; 8 of 127) ($P < 0.05$). Blood tests for cysticercosis by EITB were also performed on all patients and control subjects. Tests were repeated in subjects in whom results were ambiguous, the ELISA test was positive and EITB test negative, or even in whom both tests were negative if they had a history of seizures. In 29 patients, blood samples (18.35%; 29 of 158) were positive for antibodies against at least one of the seven antigens. EITB assays repeated because of an ambiguous result always proved negative, and in our experimental conditions, all ELISA-negative samples were confirmed negative by EITB. Again, no differences in terms of gender, socioeconomic status, or place of origin were observed between EITB-positive and EITB-negative patients. In 2 control subjects (1.57%; 2 of 127), a positive EITB result was obtained. There was therefore an appreciable difference in the prevalence of antibodies against *Taenia solium* metacestode in the two groups.

The most common psychiatric conditions of the patients showing positive ELISA and EITB results were schizophrenia and organic mental illness, although the rates of these disorders were similar for the entire patient population (Table 1). Patients diagnosed with mental retardation were more likely to show a positive ELISA (RR 2.16; 95% CI, 1.17 < 2.16 > 3.98; $P < 0.05$) and EITB (RR 2.92; 95% CI, 1.22 < 2.92 > 7.0; $P < 0.05$) test than the remaining patients (Table 1 and Figure 3).

A large proportion of the patients had at least one NCC-associated sign or symptom (70%), although this proportion was not higher for the patients with positive blood tests (Table 2). Dizziness, loss of memory, and blurry vision were associated with ELISA and EITB seropositivity (Table 2).

<table>
<thead>
<tr>
<th>Psychiatric diagnosis</th>
<th>Total no. patients</th>
<th>Patients showing a positive test</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ELISA-positive</td>
<td>EITB-positive</td>
</tr>
<tr>
<td>Organic mental illness</td>
<td>54/158 (34.2%)</td>
<td>19/51 (37.3%) 9/29 (31.1%)</td>
</tr>
<tr>
<td>Drug-use disorders</td>
<td>7/158 (4.4%)</td>
<td>2/51 (3.9%)</td>
</tr>
<tr>
<td>Schizophrenia</td>
<td>66/158 (41.8%)</td>
<td>19/51 (37.3%) 13/29 (44.8%)</td>
</tr>
<tr>
<td>Schizoaffective disorders</td>
<td>1/158 (0.6%)</td>
<td>1/51 (2.0%)</td>
</tr>
<tr>
<td>Mood disorders</td>
<td>23/158 (14.6%)</td>
<td>6/51 (11.8%) 4/29 (13.8%)</td>
</tr>
<tr>
<td>Sleep disorders</td>
<td>1/158 (0.6%)</td>
<td></td>
</tr>
<tr>
<td>Mental disability</td>
<td>6/158 (3.8%)</td>
<td>4/51 (7.8%) 3/29 (10.3%)</td>
</tr>
</tbody>
</table>

Parasites in stools. No *Taenia* spp. ova were detected in the 61 patient specimens examined. Nevertheless, infections by other soil-transmitted intestinal helminths were detected in high proportions: trichuriasis (95.1%; 58 of 61), ascariasis (60.7%; 37 of 61), and uncinariasis (0.5%; 1 of 61). Taeniasis was diagnosed in one control subject (0.8%; 1 of 127) and rates for trichuriasis (33.9%; 43 of 127), ascariasis (22.4%; 28...
of 127), and uncinariasis (no cases) were significantly lower than in the patients. No other platyhelminths were detected in psychiatric or control subjects.

**DISCUSSION**

In this study, ELISA was used to detect antibodies that would indicate the exposure of these psychiatric patients to *Taenia solium* at any stage prior to the time of serological testing. ELISA seroprevalence in our patient population was appreciably high (32.28%) compared with the group of control subjects or to rates cited for population surveys conducted in endemic areas. This high incidence and the lack of reports of other platyhelminths in this region point to a high degree of contact with *Taenia solium* at one or more stages in its life cycle.

The similar ELISA seroprevalences noted in the patients indicate similar exposure levels for rural and urban areas. Neither were seroprevalences affected by socioeconomic status, although most of our patients belonged to the poorest classes. However, the literature lacks epidemiologic studies examining anti-*Taenia solium* antibodies in psychiatric inpatient populations; our data are consistent with those from open population surveys. Nonetheless, the relationship detected here between the seroprevalence and the origin and socioeconomic class of the patients is significant in that it identifies the possibility of investigating the link between exposure to *Taenia solium* and the place of origin of the patients; our findings may also reflect the intervention of other factors, related to patient behavior and current life conditions. In Latin America, rates of cysticercosis as determined by EITB range from 4.9% to 22.6% for population studies, and the range is even broader in neurologic patients. In this study, 18.35% of the inpatients evaluated (29 of 158) presented anti-*Taenia solium* metacestode antibodies. Although cysticercosis in psychiatric inpatients had not been documented until now, our comparison with controls demonstrated a high seroprevalence among these subjects from a psychiatric institution in our country. This prevalence could possibly be even higher if we consider that some cases are undetectable by this immunologic test. Furthermore, if our assumption regarding the possible exposure to parasites is accurate, many exposed patients (57%; 29 of 51 of the patients showing a positive ELISA test) are likely to develop cysticercosis.

Although many patients presented clinical manifestations associated with NCC, their clinical records never showed NCC as a causal or associated organic disorder. The significance of our findings and the occurrence of NCC in these patients remain unknown, but our results suggest that a significant number of individuals acquired NCC and that this could be the cause of the specific and severe forms of mental illness observed. Hence, as recommended by other authors, a diagnosis of NCC is essential when evaluating psychiatric disorders, because it can be common in patients from endemic areas and its impact on psychiatric status cannot be ruled out.

Mentally disabled patients carry an increased risk of parasite exposure and, therefore, of developing cysticercosis. The individuals with life long cognitive limitations might be at increased risk for parasite exposure and the early or delayed appearance of this limitations is a factor that must necessarily be taken into account when assessing the development of *Taenia solium* in psychiatric patients. Measures aimed at improving the living conditions of mentally disabled patients must be systematically supervised, because taeniasis and cysticercosis can result from exposure to parasites in conditions of inadequate health care, hence worsening these patients’ already precarious living conditions. In endemic countries, the mentally disabled should be therefore considered a high-risk group for *Taenia solium* infection. In these patients, exposure could occur in the family setting, in conditions promoting the transmission of *Taenia solium*, or even in public health centers, where limited resources condition the quality of medical services and conditions are such that infections may persist.

Finally, despite the high number of seropositive patients for the ELISA and Western blot tests in the absence of diagnosed cases of neurocysticercosis, our study indicates underdiagnosing of taeniasis and cysticercosis in these psychiatric inpatients such that the burden of this disease is not clearly known. Establishing the association between symptomatic cysticercosis and mental disorders will require studies on series of psychiatric patients focusing on the early diagnosis of these infections, analysis of parasite exposure, and evaluation of risk factors. This will allow the study of the association of symptomatic cysticercosis with the mental disorders and the design of epidemiologic measures aimed at interrupting the chain of transmission of the parasites.

**TABLE 2**

Clinical manifestations of neurocysticercosis in ELISA-positive and EITB-positive patients

<table>
<thead>
<tr>
<th>Clinical manifestations</th>
<th>Total no. patients</th>
<th>% ELISA-positive</th>
<th>Relative risk (95% CI; <em>P</em>&lt;0.05)</th>
<th>% EITB-positive</th>
<th>Relative risk (95% CI; <em>P</em>&lt;0.05)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>83/158 (52.5%)</td>
<td>17/51 (33.3%)</td>
<td>NR</td>
<td>10/29 (34.5%)</td>
<td>NR</td>
</tr>
<tr>
<td>Dizziness</td>
<td>64/158 (40.5%)</td>
<td>27/51 (52.9%)</td>
<td>1.65;1.05 &lt; RR &gt; 2.59</td>
<td>17/29 (58.6%)</td>
<td>2.08; 1.07 &lt; RR &gt; 4.06</td>
</tr>
<tr>
<td>Blurry vision</td>
<td>64/158 (40.5%)</td>
<td>28/51 (54.9%)</td>
<td>1.79;1.14 &lt; RR &gt; 2.81</td>
<td>17/29 (58.6%)</td>
<td>2.08; 1.07 &lt; RR &gt; 4.06</td>
</tr>
<tr>
<td>Vomiting</td>
<td>26/158 (16.4%)</td>
<td>8/51 (15.7%)</td>
<td>NR</td>
<td>5/29 (17.2%)</td>
<td>NR</td>
</tr>
<tr>
<td>Memory loss</td>
<td>82/158 (51.9%)</td>
<td>37/51 (72.5%)</td>
<td>2.45;1.44 &lt; RR &gt; 4.16</td>
<td>21/29 (72.4%)</td>
<td>2.43; 1.15 &lt; RR &gt; 5.16</td>
</tr>
<tr>
<td>Tremors</td>
<td>44/158 (27.9%)</td>
<td>18/51 (35.3%)</td>
<td>NR</td>
<td>11/29 (37.9%)</td>
<td>NR</td>
</tr>
<tr>
<td>Syncope</td>
<td>41/158 (25.9%)</td>
<td>23/51 (45.1%)</td>
<td>NR</td>
<td>11/29 (37.9%)</td>
<td>NR</td>
</tr>
<tr>
<td>Seizures</td>
<td>20/158 (12.7%)</td>
<td>9/51 (17.6%)</td>
<td>NR</td>
<td>6/29 (20.7%)</td>
<td>NR</td>
</tr>
</tbody>
</table>

NR, Nonrelevant relative risk.

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Table 3
Psychiatric diagnoses and clinical manifestations of neurocysticercosis in EITB-positive patients

<table>
<thead>
<tr>
<th>Clinical manifestations</th>
<th>Organic mental illness</th>
<th>Schizophrenia</th>
<th>Mood disorders</th>
<th>Mental disability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptoms</td>
<td>6/9 (66.7%)</td>
<td>10/13 (76.9%)</td>
<td>3/4 (75.0%)</td>
<td>2/3 (66.7%)</td>
</tr>
<tr>
<td>Headache</td>
<td>3/9 (33.3%)</td>
<td>4/13 (30.1%)</td>
<td>2/4 (50.0%)</td>
<td>1/3 (33.3%)</td>
</tr>
<tr>
<td>Dizziness</td>
<td>5/9 (55.6%)</td>
<td>8/13 (61.5%)</td>
<td>2/4 (50.0%)</td>
<td>2/3 (66.7%)</td>
</tr>
<tr>
<td>Blurry vision</td>
<td>6/9 (66.7%)</td>
<td>8/13 (61.5%)</td>
<td>1/4 (25.0%)</td>
<td>2/3 (66.7%)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>1/9 (11.1%)</td>
<td>4/13 (30.7%)</td>
<td>0/4 (0.0%)</td>
<td>0/3 (0.0%)</td>
</tr>
<tr>
<td>Memory loss</td>
<td>5/9 (55.6%)</td>
<td>10/13 (76.9%)</td>
<td>4/4 (100.0%)</td>
<td>2/3 (66.7%)</td>
</tr>
<tr>
<td>Tremors</td>
<td>4/9 (44.4%)</td>
<td>4/13 (30.8%)</td>
<td>2/4 (50.0%)</td>
<td>1/3 (33.3%)</td>
</tr>
<tr>
<td>Syncope</td>
<td>3/9 (33.3%)</td>
<td>6/13 (46.2%)</td>
<td>1/4 (25.0%)</td>
<td>1/3 (33.3%)</td>
</tr>
<tr>
<td>Seizures</td>
<td>3/9 (33.3%)</td>
<td>1/13 (7.7%)</td>
<td>0/4 (0.0%)</td>
<td>2/3 (66.7%)</td>
</tr>
</tbody>
</table>

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REFERENCES
26. Tsang VC, Brand JA, Boyer AE, 1989. An enzyme-linked im-
munoelectrotransfer blot assay and glycoprotein antigens for diagnosing human cysticercosis (Taenia solium). J Infect Dis
159: 50–59.
93–110.
677–685.