SHORT REPORT

Is dementia reversible in patients with neurocysticercosis?

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Objective: To determine the correlates and outcome of dementia in patients with neurocysticercosis (NCC).

Methods: Ninety consecutive patients with untreated NCC underwent a cognitive assessment (Mini-mental State Examination, Neurobehavioral Cognitive Status Examination, and IQCODE) and were classified as having or not having dementia according to DSM-IV criteria. Imaging and cerebrospinal fluid examination data were recorded. The cognitive measures were repeated six months after treatment with albendazole and steroids.

Results: At the initial evaluation 15.5% (n = 14) of the patients were classified as having dementia. Dementia was associated with older age, lower education level, increased number of parasitic lesions in the brain (mostly in the frontal, temporal, and parietal lobes). After six months, 21.5% of the patients from the dementia group continued to have a full dementia disorder and 78.5% no longer fulfilled the DSM-IV criteria for dementia, although some of these patients still showed mild cognitive decline.

Conclusions: The results of this study suggest that dementia occurs frequently in patients with untreated NCC, and it is reversible in most cases.

It is well known that neurocysticercosis (NCC), the commonest parasitic brain disease,[1][2] causes epilepsy, focal neurological signs, intracranial hypertension, and stroke.[3][4] Although the neuropsychiatric dimension of NCC was reported many years ago,[5] only recently has it been systematically studied. In a series of 38 outpatients with NCC, Forlenza *et al*[6] found that 87.5% of patients had cognitive disturbances and 15.6% had severe cognitive abnormalities. However, the authors did not specify if those patients were cases of dementia, mental retardation, or delirium. Other studies that have reported dementia in patients with NCC[7–11] have been mostly case reports, retrospective case series, or studies lacking a systematic cognitive evaluation.

The aims of our study were:

- to determine the correlates of dementia in patients with previously untreated NCC
- to evaluate the reversibility of cognitive decline after treatment.

METHODS

We included untreated patients with a definitive diagnosis of NCC according to the diagnostic criteria developed by Del Brutto *et al*.[12] Patients between 18 and 70 years of age were consecutively recruited over a one year period from the clinical services of the National Institute of Neurology and Neurosurgery at Mexico City (including outpatients and hospitalised patients from the neurology and psychiatry wards) after obtaining informed consent from the patients or their relatives. The institutional ethics committee revised and approved the protocol. Patients with other relevant neurological or medical conditions, as well as substance abusers, were excluded from the study.

We used the Mini-mental State Examination (MMSE)[13] and the Neurobehavioral Cognitive Status Examination (COGNISTAT), a well validated test previously used in patients with neurological disorders to assess all the patients.[14][15] Both tests were performed only if the patient was not in a postictal period. We also used the Informant Questionnaire on Cognitive Decline (IQCODE), which provides information regarding social functioning and compares the subject with him or herself, according to an interview with the relatives,[16][17] to discriminate between current cognitive decline and constitutional mental retardation. Two independent neuropsychiatrists classified the patients as having or not having a dementia disorder according to DSM-IV criteria.[18] The Delirium Rating Scale (DRS)[19] was used to identify cases of cognitive decline related to delirium. All patients underwent cerebrospinal fluid (CSF) and neuroimaging studies (CT and MRI) within a period of two weeks before or after the cognitive assessment. Imaging studies were assessed by a neuroradiologist blinded to the rest of the study. Electroencephalographic recordings were indicated only in patients with seizures, and these were undertaken in 48 patients (53.3% of the total sample).

All patients with active NCC received a standard treatment with steroids and albendazole, with standard dosages (15 mg/kg per day). Six months after the initial evaluation, we repeated the cognitive tests in all patients classified as having a dementia disorder.

We analysed the distribution of numerical variables by means of the Kolmogorov–Smirnov test to decide whether to use parametrical or non-parametrical tests. We performed descriptive statistics, as well as a bivariate analysis for comparing patients with dementia with those without a cognitive disorder (Mann–Whitney test for numerical variables (because of non-normal distribution of variables), and Pearson's χ^2 tests for nominal variables whenever the sample size permitted it); in cases with expected values <5 in the contingency tables, we used Fisher's exact test. Also, considering the ordinal nature of neuropsychological variables in this study, we used Wilcoxon's test for related samples to compare the ratings on the COGNISTAT and MMSE before and after treatment.

RESULTS

A total of 90 patients with untreated NCC were included in the study. Dementia was present in 15.5% of the subjects (n = 14) at the time of the initial evaluation according to DSM-IV criteria. The DRS scores in these patients had a median of 5 with a range between 4 and 6 in all cases below suggested cut-offs for delirium. Twenty patients (22.2%) also

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Abbreviations: COGNISTAT, Neurobehavioral Cognitive Status Examination; DRS, Delirium Rating Scale; IQCODE, Informant Questionnaire on Cognitive Decline; MMSE, Mini-mental State Examination; NCC, neurocysticercosis

Table 1 Comparison of the clinical and neuroimaging characteristics of patients with and without dementia in an untreated neurocysticercosis population

Variable	Patients with dementia (n = 14)	Patients without dementia (n = 68)	OR (95% CI)	p value
Age in years, median (range)	63 (27–69)	33 (17–69)	–	0.001†
Education level in years, median (range)	2 (0–12)	9 (0–16)	–	0.007†
Male sex	8 (57%)	34 (50%)	1.3 (0.4 to 4.2)	0.626‡
Presence of epilepsy	12 (85%)	40 (58%)	4.2 (0.8 to 20.2)	0.057‡
Presence of active neurocysticercosis	12 (85%)	52 (76%)	1.8 (0.3 to 9.1)	0.724‡
No of parasitic lesions, median (range)	36 (3–43)	3 (0–85)	–	<0.001†
Frontal	12 (85%)	32 (47%)	6.7 (1.4 to 32.4)	0.008‡
Temporal	12 (85%)	34 (50%)	6 (1.2 to 28.8)	0.014‡
Parietal	12 (85%)	28 (41%)	8.5 (1.7 to 41.3)	0.002‡
Occipital	8 (57%)	18 (26%)	3.7 (1.1 to 12.1)	0.054¶
Presence of vascular lesions (stroke)	2 (14%)	2 (2%)	5.5 (0.7 to 42.9)	0.073¶
Presence of Cysticercus racemosus	0 (0%)	14 (20%)	0.79 (0.70 to 0.89)	0.113¶
Presence of arachnoiditis	4 (28%)	16 (23%)	1.3 (0.35 to 4.71)	0.736¶
Intracranial pressure*	140 (90–170)	145 (50–290)	–	0.961†
Cerebrospinal fluid variables, median (range)				
Proteins*	32 (23–123)	34 (12–105)	–	0.349†
Cells*	9 (0–521)	9 (.346)	–	0.346†
Glucose*	54 (45–65)	51 (13–118)	–	0.226†

In the case of numerical variables, the data are expressed in terms of medians and extreme values, given the abnormal distribution according to the Kolmogorov–Smirnov test.

Patients with delirium (n = 8) were excluded from this analysis because it would have introduced a considerable heterogeneity into the group of patients without dementia.

*The sample size of the non-demented group for these four variables is only 64 (four patients from this group showed clinically significant intracranial hypertension and thus were not considered for lumbar puncture).
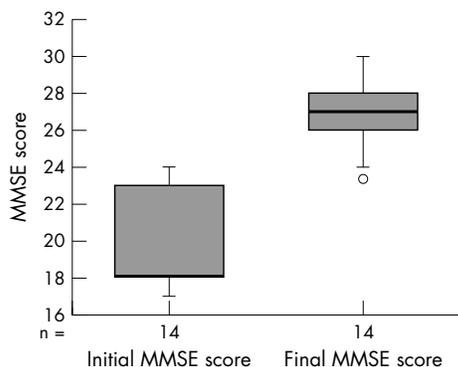
†Mann–Whitney test, ‡Pearson's χ^2 test, ¶Fisher's exact test.

had minor forms of cognitive disturbance as revealed by direct mental examination (COGNISTAT). However, they had normal ratings in the indirect examination (IQCODE), so it is difficult to say if these minor forms of cognitive dysfunction were in fact the result of NCC per se or constitutional intellectual disturbances.

Comparison between patients with and without dementia (table 1) revealed that those with dementia were older and had lower educational levels. Regarding neuroimaging data, patients with dementia not only had greater numbers of parasitic lesions, but also a higher proportion of lesions located in the frontal, parietal, and temporal lobes. We observed a tendency for the presence of parasitic lesions in the occipital lobes and the findings of vascular (ischaemic) and epileptic complications of NCC. CSF variables were not

Figure 1 In our sample of demented patients with neurocysticercosis, Mini-mental State Examination (MMSE) scores improved significantly after medical treatment with albendazole and steroids (p = 0.001, Wilcoxon's test for related samples), as shown in the box plots. The horizontal lines across the boxes reflect the median of MMSE scores: 18 at baseline and 27 at final assessment; the boxes represent the interquartile range which contains the 50% of values. The whiskers extend to the highest and lowest MMSE scores, excluding outliers, and the circle represents an outlying value.

significantly different between the groups. Patients were also classified as having or not having active NCC according to classical criteria.[9] We found no significant difference between demented and non-demented patients regarding this variable. There was also no significant difference between the groups with regard to presence of arachnoiditis (as defined by MRI data, increased mononuclear cells and proteins, and a positive immunological test for cysticercosis in CSF).

Six months after baseline assessments, the dementia group had the following outcomes. Three patients (21.5%) continued to have a dementia disorder. Two of them had inactive forms of NCC and therefore did not receive antiparasitic treatment. They neither showed improvement nor had cognitive worsening. Eleven patients (78.5%) no longer fulfilled the DSM-IV criteria for dementia, although only six of these patients showed complete recovery. The remaining five patients still had mild forms of cognitive disturbance, as defined by mild to moderate isolated deficits at second evaluation on one of the following domains of the COGNISTAT: attention, language, constructional abilities, memory, calculation abilities, reasoning. All cognitive functions assessed with the COGNISTAT in the group of demented patients showed significant improvement after treatment: orientation (p = 0.010), attention (p = 0.005), comprehension of oral language (p = 0.008), verbal repetition (p = 0.016), naming (p = 0.016), constructional abilities (p = 0.006), verbal memory (p = 0.002), calculation abilities, (p = 0.006), reasoning/analogies (p = 0.010), and reasoning/judgement, (p = 0.007). Figure 1 shows the MMSE scores before and after treatment.

DISCUSSION

The results of the cross-sectional phase of our study suggest that dementia syndrome observed in patients with NCC could be a combined effect, resulting from multiple parasitic and vascular lesions, disrupting frontal-parietal-temporal networks related to intellectual functioning in patients with vulnerable brains (because of repeated epileptic seizures, low educational levels, advanced age). This view is compatible with previous descriptions,[6 7 11 12] and emphasises the

multifactorial nature of dementia in this particular population, intrinsically related to biological and clinical heterogeneity of NCC. Regarding particular cases, it is possible to come across not only older patients with low education and Alzheimer-like decline, but also young patients with subacute or chronic cognitive dysfunction, accompanied by seizures, headache, or focal neurological deficits.

Is dementia reversible in patients with NCC? The longitudinal phase of our study shows that most patients treated with a regular pharmacological regimen experience noticeable recovery of cognitive functioning, although some continue to have minor forms of intellectual disturbance, mainly in constructional and calculation abilities. This is similar to the course of other clinical features of NCC after treatment, as happens with epileptic seizures.[20] This fact highlights the importance of the sustained inflammatory and other immunological mechanisms behind the clinical picture of NCC, and the probable benefits of both anticysticercal and anti-inflammatory pharmacological treatments.[21] Once again, the biological heterogeneity of NCC could be responsible for the diverse outcomes in our sample, which could be restated as: complete or partial recovery in most cases and lack of cognitive improvement in a minority of cases.

A limitation of the present study is that we did not include a placebo controlled group. Although the probability of natural recovery in some patients is impossible to rule out completely, ethical concerns make it difficult to plan placebo controlled studies, given the evidence that NCC can be effectively treated with albendazole[22 23] or praziquantel[24 25] in combination with steroids. The main limitation of our study is the small sample size of the dementia group. Since NCC is a considerably heterogeneous disease, it is difficult to establish the precise role of each biological factor implicated in the occurrence of dementia, as well as the complete longitudinal picture. Future studies could improve upon the present observations by means of blind evaluations, more detailed and repeated imaging and electrophysiological studies (to rule out subclinical seizures), larger samples, and longer follow ups, in order to improve prognosis and clinical monitoring of treatment. At this time the outcome of dementia patients with NCC seems favourable in most cases with the use of standard pharmacological interventions.

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