INTERRELATIONSHIP BETWEEN RADIOLOGIC FINDINGS AND PROGNOSIS OF EPILEPSY IN CHILDREN WITH NEUROCYSTICERCOSIS

Lisiane Seguti Ferreira¹, Verônica A. Zanardi², Li Min Li¹, Marilisa M. Guerreiro¹

ABSTRACT - Introduction: Epileptic manifestations of Neurocysticercosis (NC) appear to depend on number and localization of the cysts. The objective of this study was to investigate the relationship between CT findings, number of parasites and the evolutive stage of the cysts, and the prognosis of epilepsy in children with NC. Method: We studied 28 patients with the parenchymal form of NC, considering: epilepsy duration; seizure frequency before and after AED treatment; seizure control; number of AED and recurrence after AED withdrawal. Clinical information was crossed with the number of lesions and disease activity in univariate comparison. Results: The analysis of the clinical data in relation to the number of lesions and disease activity showed no statistical difference among the variables (p>0.05). Conclusion: We conclude that the course of epilepsy due to NC in childhood cannot be based exclusively on the number or stage of the parasites.

KEY WORDS: neurocysticercosis, childhood epilepsy, radiology, prognosis.

METHOD
This was a retrospective study. We selected all patients with less than 16 years with probable or definitive diagnosis for NC according to Del Bruto et al.¹¹. Forty-one pa-
tients with NC were followed at the Pediatric Epilepsy Out-
patient Clinic at the University of Campinas from January
1983 to January 1999. Five patients had a single seizure
with follow-up of at least 12 months. Eight patients had
the encephalitic form of NC. These 13 patients were exclu-
ded because single seizure is not epilepsy, and the ence-
phalitic form is a more severe presentation of NC with a
tendency for permanent neurological sequelae and severe
epileptic condition than the one habitually found in pa-
tients with epilepsy resulting from NC.

We obtained all information from the remaining 28
patients on revision of their medical records, complemen-
ted with direct interview with patients and guardians when-
ever possible. A semi-structured protocol was filled in
for every patient, considering: epilepsy duration (this was
defined as the period between the first seizure up to the
moment that antiepileptic drugs (AED) were withdrawn
or until the last appointment for patients with persistent
seizures, regardless of any remission period during the
follow-up); seizure frequency before AED treatment was
classified according to the total number of seizures quan-
tified as: A<10, B = 10 to 50, C>50; seizure frequency
after AED introduction (same classification as above); sei-
zure control was defined as one year without having sei-
zures; number of AED to obtain seizure control; recurrence
after AED withdrawal (the policy of AED withdrawal was
 carried out after two years of seizure-freedom).

All 28 patients had computerized tomography scan
(CT) at the time of the diagnosis in our center. All exams
were revised by one of us (VAZ), a neuroradiologist with
experience with NC. Lesions were counted and classified
into three groups: five or less, between six and 10, and
more than 10. Patients with a single calcification were
excluded from this research. The disease activity was clas-
sified as active (appears on CT as hipodense cyst without
enhancement), transitional (there is a ring or nodular con-
trast enhancement), and inactive (calcified lesions on CT)
based on the viability of the parasite as proposed by Carpio
et al.12. When lesions in different stages were found in the
same patient, they were classified according to the most
active lesion detected.

The clinical information listed above was crossed with
the number of lesions and disease activity in univariate
comparison using Kruskal-Wallis with post hoc pairwise
comparison or Fisher exact test, and significance was as-
sumed when p<0.05.

RESULTS

Twenty-eight patients (16 girls, mean age = 7.2
years, mean follow-up of 64.5 months) had paren-
chymal form of NC and normal neurological exami-
nation and were the subjects of this study.

Concerning the evolutive stage of the parasite,
17 patients were at inactive phase, six at transitional
phase and five children had active lesions on CT.
Regarding number of lesions, 18 patients had five
or less than five lesions, four had between six and
10 lesions, and six had more than 10 cysts.

The statistical analysis of clinical data in relation
to the number of lesions and disease activity showed
the following.

Epilepsy duration: mean duration of epilepsy was
7.2 years (range from 2.3 to 14.1 years). We did not
find any statistical difference when we compared
mean scores of epilepsy duration with stage (Kruskal-
Wallis test p=0.20) and number of lesions (Kruskal-
Wallis test p=0.18). Multiple cysts, regardless of
stage, did not influence epilepsy duration and had
the same behavior as a few lesions.

Seizure frequency: 12 patients had less than 10
seizures, 10 children had seizures between 10 and
50, and six had more than 50 seizures. We did not
find statistical difference comparing

<table>
<thead>
<tr>
<th>Seizure frequency</th>
<th>Number of lesions</th>
<th>Disease activity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>≤ 5</td>
<td>5-10</td>
</tr>
<tr>
<td>A (&lt; 10)</td>
<td>10</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>35.7%</td>
<td>3.5%</td>
</tr>
<tr>
<td>B (10-50)</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>17.9%</td>
<td>7.1%</td>
</tr>
<tr>
<td>C (&gt; 50)</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>10.7%</td>
<td>3.5%</td>
</tr>
</tbody>
</table>

Seizure frequency and number of lesions Fisher’s exact test p 0.43
Seizure frequency and disease activity Fisher’s exact test p 0.42
Table 2. Seizure frequency after AED introduction.

<table>
<thead>
<tr>
<th>Seizure frequency</th>
<th>Number of lesions</th>
<th>Disease activity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>≤ 5</td>
<td>5-10</td>
</tr>
<tr>
<td>A &lt; 10</td>
<td>12</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>42.9%</td>
<td>7.1%</td>
</tr>
<tr>
<td>B 10-50</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>14.3%</td>
<td>3.6%</td>
</tr>
<tr>
<td>C &gt; 50</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>7.1%</td>
<td>3.6%</td>
</tr>
</tbody>
</table>

Seizure frequency after AED and number of lesions: Fisher's exact test p 0.17
Seizure frequency after AED and disease activity: Fisher's exact test p 0.33

Table 3. Number of AEDs.

<table>
<thead>
<tr>
<th>Number of drugs</th>
<th>Number of lesions</th>
<th>Disease activity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>≤ 5</td>
<td>5-10</td>
</tr>
<tr>
<td>1</td>
<td>8</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>28.6%</td>
<td>3.6%</td>
</tr>
<tr>
<td>2</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>21.4%</td>
<td>14.3%</td>
</tr>
<tr>
<td>≥ 3</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>14.3%</td>
<td>10.7%</td>
</tr>
</tbody>
</table>

Number of AED and number of lesions: Fisher's exact test p 0.06
Number of AED and disease activity: Fisher's Exact Test p 0.52

Table 4. Seizure control.

<table>
<thead>
<tr>
<th>Seizure control</th>
<th>Number of lesions</th>
<th>Disease activity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>≤ 5</td>
<td>5-10</td>
</tr>
<tr>
<td>Yes</td>
<td>17</td>
<td>3</td>
</tr>
<tr>
<td>n = 24</td>
<td>60.7%</td>
<td>10.7%</td>
</tr>
<tr>
<td>No</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>n = 4</td>
<td>3.6%</td>
<td>3.6%</td>
</tr>
</tbody>
</table>

Control seizure and number of lesions: Fisher's exact test p 0.16
Control seizure and disease activity: Fisher's exact test p 0.40

in univaried analysis seizure frequency after AED with stage and number of lesions (Table 2).

Number of AED: nine patients received only one AED during their treatment, 10 received two AED, and nine received three or more AED, either isolated or in association. There was no statistical difference comparing number of AED with stage and number of lesions (Table 3).

Seizure control: 24 patients obtained control of their epilepsy. The mean time to obtain control was 16.1 months. We did not find any difference when we compared seizure control with the stage and number of lesions (Table 4).

Recurrence: it occurred in 13 out of 24 evaluated patients. The mean time to seizure recurrence was 21.4 months, ranging from one to 48 months. There was no statistical difference when comparing recurrence with the stage and number of lesions (Table 5).
DISCUSSION

Neuroimaging has attained enormous progress during last decade. CT is very helpful in NC because it is a safe, precise and noninvasive method with more than 95% accuracy to define number, localization and evolutive stages of the parasites, especially in the parenchymal form of the disease. In developing countries where MRI machines are not always available, and considering the fact that calcifications are the main radiologic finding in NC, CT is still the most performed and useful examination.

In this study, we tried to correlate CT findings (number and evolutive stages of lesions) with prognostic factors such as epilepsy duration, seizure frequency before and after AED introduction, number of AED, seizure control and seizure recurrence. In unvaried analysis, we did not find any correlation among them. When isolated, neither number of parasites nor their stages are predictive factors of outcome. In this series, we observed seizure-free patients with multiple lesions in contrast to patients with refractory epilepsy with few lesions.

One limitation of our research is the low number of patients, which is due to the rigid inclusion criteria. However, out of 12 analyzed factors, only two showed borderline findings: number of lesions with recurrence (p=0.08) and number of lesions with number of AED (p=0.06). If number of patients were higher, there would be a chance that statistical analysis could show different data of the two variables described above. Some authors found that patients with calcified lesions in large number have a worse prognosis, while other authors have different point of view.

The poor understanding of the pathophysiology of the seizures due to NC parallels difficulties in explaining the variability of clinical manifestations. Particularly in childhood, presentation may vary from “benign” to severe epileptic syndromes, such as Lennox-Gastaut syndrome. Some factors that may contribute to explain this variability are: spontaneous resolution of the lesions; persistence of perilesional edema around calcified lesions; unpredictable evolution of the parasite that allows the coexistence of different forms in the same subject; the immune response of the host; and, the environment in which the child lives which may be responsible for new infestations.

The severity of clinical manifestation has also been correlated to HLA antigens in the surface of the parasites, which suggests a genetic influence in the presentation of NC. Del Bruto found higher rates of HLA 28 in patients with NC when compared to controls. Another antigen, DQW2, may be related to the resistance of the disease. Therefore, an individual predisposition to develop parenchymal NC is likely to occur and could in part explain the variability of the clinical expression.

We conclude that the course of epilepsy due to NC in childhood cannot be based exclusively on the number or stage of the parasites. Patients with multiple lesions will not necessarily present more seizures or need more drugs than the others. Intrinsic characteristics of the parasites as well as immune genetic aspects may play important role in the explanation of the pleomorphic and unpredictable course of the clinical picture.

Acknowledgements - The authors thank Mrs. Cleide Moreira Silva for statistical support.

REFERENCES