Longer epilepsy duration and multiple lobe involvement predict worse seizure outcomes for patients with refractory temporal lobe epilepsy associated with neurocysticercosis

Longa duração de epilepsia e envolvimento de múltiplos lobos são fatores preditivos de pior controle das crises convulsivas em pacientes com epilepsia refratária do lobo temporal associada a neurocisticercose

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ABSTRACT

Objective: To investigate the surgical outcomes of temporal lobe epilepsy associated with hippocampal sclerosis (TLE-HS) and neurocysticercosis (NCC). Methods: A retrospective investigation of patients with TLE-HS was conducted in a tertiary center. Results: Seventy-nine (62.2%), 37 (29.1%), 6 (4.7%), and 5 (3.9%) patients were Engel class I, II, III, and IV, respectively. Fifty-two (71.2%) patients with epilepsy durations ≤ 10 years prior to surgery were seizure-free 1 year after the operation compared to 27 (50.0%) patients with epilepsy durations > 10 years (p = 0.0121). Forty-three (72.9%) patients with three or fewer lobes affected by NCC were seizure-free one year after the operation, and 36 (52.9%) patients with more than three involved lobes were seizure-free after surgery (p = 0.0163). Conclusions: Longer epilepsy durations and multiple lobe involvement predicted worse seizure outcomes in TLE-HS plus NCC patients.

Keywords: temporal lobe epilepsy, hippocampal sclerosis, neurocysticercosis.

RESUMO

Objetivo: Investigar o resultado cirúrgico da epilepsia do lobo temporal associada à esclerose hipocampal (TLE-HS) e neurocisticercose (NCC). Métodos: Estudo retrospectivo realizado em um centro de epilepsia. Resultados: Cinquenta e dois pacientes (71,2%) com 10 anos ou menos de epilepsia antes da cirurgia tornaram-se livres de crises após um ano da operação, enquanto que 27 (50,0%) com mais de dez anos tornaram-se livres de crises após cirurgia (p = 0,0121). Quarenta e três pacientes (72,9%), com três ou menos lobos afetados pela NCC tornaram-se livres de crises após um ano de operação, enquanto que 36 pacientes (52,9%) com mais de três lobos envolvidos estavam livres de crises após a cirurgia (p = 0,0163). Conclusão: A duração mais longa da epilepsia e o envolvimento de múltiplos lobos prevê pior resultado após a cirurgia para TLE-HS mais NCC.

Palavras-chave: epilepsia do lobo temporal, esclerose hipocampal, neurocisticercose.

Neurocysticercosis (NCC) is an infection of the central nervous system in which the meninges are infected with the larval stage of the pork tapeworm *Taenia solium*²,³. This tapeworm is endemic in the majority of low-income countries in which pigs are raised and continues to be one of the most important causes of seizures in the world⁴,⁵. The World Health Organization (WHO) lists NCC as a neglected tropical disease and estimates that approximately 50 million

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people worldwide have NCC and that it causes approximately 50,000 deaths each year. Recent Brazilian investigations have reported that NCC seems to contribute or even cause refractory epileptic seizures associated with hippocampal sclerosis. According to these investigations, inflammatory and/or electrogentic mechanisms promoted by NCC may induce epileptogenic discharges.

In the present study, we investigated the surgical outcomes of patients with temporal lobe epilepsy associated with hippocampal sclerosis and NCC.

METHODS

Study delineation

A retrospective observational investigation was conducted with data collected from all patients treated in the epilepsy clinic of the Faculdade de Medicina de Sao Jose do Rio Preto (FAMERP, a Brazilian tertiary referral epilepsy center) with diagnoses of temporal lobe epilepsy associated with hippocampal sclerosis (TLE-HS) from January 2000 to March 2013. The clinical data were retrospectively obtained from the patient records and files. For all patients with a diagnosis of TLE-HS based on magnetic resonance imaging (MRI), the following data were collected: sex, age at surgery, handedness, type and number of antiepileptic drugs (AEDs) used, and formal neuropsychological evaluation results. NCC was evaluated with brain computed tomography (CT). The present study was approved by the ethical committee of our institution.

Pre-surgical evaluation

The patients were submitted to video-electroencephalography (EEG) monitoring using Neuro Workbench software and Nihon Kohden hardware to record all epileptic events for later evaluation. Patient data were analyzed by an experienced epileptologist as an integral part of the inpatient assessment.

All patients submitted to pre- and post-surgical (at 12 months) neuropsychological assessments. Verbal memory was assessed with a list-learning task, and figural memory was assessed with a learning test involving independent items. Memory deficits were defined by performances that were one standard deviation below the normal performance of age-matched controls.

Brain MRI was performed obtained according to a specific epilepsy protocol using a Philips 1.5-Tesla scanner at the Department of Neuroradiology of our institution. All MRI data were analyzed by an experienced neuroradiologist who confirmed the visual radiological diagnoses of TLE-HS. NCC was evaluated with brain CT, and the number of involved lobes was documented. All patients underwent MRI within 30 days of surgery and at each year of follow-up.

Biopsy specimens were collected from all patients with chronic drug-resistant TLE-HS with radiological evidence who underwent surgery. Standardized neuropathological analyses were performed for all studied patients. The surgical specimens submitted for neuropathological evaluation were microscopically analyzed using hematoxylin-eosin staining. The pathologists reported their findings blind to the clinical and imaging data.

Surgical technique

The surgical approaches were similar for all patients, and a single neurosurgeon who was experienced with epilepsy surgery (SCS Jr.) performed all of the procedures. The patient positioning included the placement of a shoulder roll to elevate the trunk followed by turning of the head 15-20 degrees from the midline so that the operative side was facing up. The head was slightly extended to bring the sylvian fissure to a plane that was perpendicular to the operating approach. Finally, the vertex was dropped down toward the floor to improve the surgeon's access to the mesial structures and allow for less temporal lobe retraction. A reverse question mark incision was made from immediately above the zygoma and extending back into the temporal region. An anterior temporal craniotomy was performed respecting the anatomical landmarks of the temporal lobe from the root of the zygoma to the anatomic keyhole. The remaining anterior and lateral bone was removed by drilling down to the limits of the medial fossa floor. At the end of the craniotomy, all of the bone edges were waxed as necessary, any exposed air cells were sealed, and take-up sutures were performed prior to opening the dura mater to prevent epidural bleeding. A maximum of 4.0 to 5.0 cm of the anterior lateral temporal lobe was resected. The mesial resection included removal of the amygdala and the anterior 2.0 to 3.0 cm of the hippocampus.

Outcome assessments and follow-up

Follow-up investigations were performed on the operated patients. At the 12-month follow-up, all patients underwent a neurological examination that included observations of behavior disorders, explorations of seizure outcomes and 1.5-Tesla cerebral MRI. Seizure outcomes were classified according to the Engel classification.

Ethical statement

The ethical committee of our institution analyzed the project and approved the investigation. This study complied with the Declaration of Helsinki. Informed consent was acquired from all patients and/or guardians.

Statistical analysis

The data collected from all patients were organized in tables. The data are expressed as the means ± the SDs for parametric variables and the median values for nonparametric variables. Statistical analyses were performed with Fisher’s exact tests. A p-value < 0.05 was considered statistically significant.
RESULTS

A total of 136 patients with medically intractable TLE-HS plus NCC were diagnosed and treated at our institution. However, nine patients were excluded from this sample because they did not achieve a minimum of 1 year of follow up.

Table 1 summarizes the clinical findings of 127 patients with TLE-HS plus NCC who underwent operations. There were more males than females, and the mean age at surgery was 34.7 ± 11.9 (21-68 years). The mean age at seizure onset was 14.4 ± 18.6 (8-65 years). The seizure frequency was 12.3 ± 21.2 (1-90) per month. The mean time from seizure onset to surgery was 11.8 ± 22.9 (1-33 years). Complex partial seizures were the most common type and were present in 116 (91.3%) patients, followed by generalized tonic-clonic seizures in 9 (7.1%) patients and multiple seizure types in 2 (1.6%).

Table 2 summarizes the surgical outcomes of the 127 patients with TLE-HS plus NCC who underwent surgery. After 1 year of follow up, 79 (62.2%) patients were Engel class I, 37 (29.1%) were Engel class II, 6 (4.7%) were Engel class III, and 5 (3.9%) were Engel class IV. Significant differences in the achievement of seizure freedom (Engel class I) were observed according to the time from first seizure to surgery and the number of lobes affected by NCC. First, we found that 52 (71.2%) patients with epilepsy durations ≤ 10 years prior to surgery were seizure-free (Engel I) 1 year after the operation, whereas 27 patients (50.0%) with epilepsy durations > 10 years were seizure-free (Engel class I) following surgery (Fisher’s exact test, p = 0.0121). Second, we observed that 43 patients (72.9%) with three or fewer lobes affected by NCC were seizure-free (Engel class I) 1 year after the operation, and 36 patients (52.9%) with more than three involved lobes were seizure-free (Engel class I) (Fisher’s exact test, p = 0.0163). Neither the age at the time of surgery nor the side of the operation had a significant effect. No relationship between the side of the NCC and the side of the hippocampal sclerosis was observed in the present study.

Table 3 summarizes the complications that occurred in the 127 surgical patients. A total of 18 patients (14.2%) experienced post-operative complications. Infections were observed in 14 (11.0%) patients, and 1 of these required bone removal. Two (1.6%) patients exhibited transitory contralateral hemiparesis, and two (1.6%) had clinical complications.
Table 3. Complications of 127 patients with TLE-HS plus NCC who underwent operations.

<table>
<thead>
<tr>
<th>Number of cases/</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infection</td>
<td>14/11.0</td>
</tr>
<tr>
<td>Contralateral hemiparesis</td>
<td>2/1.6</td>
</tr>
<tr>
<td>Clinical complications</td>
<td>2/1.6</td>
</tr>
<tr>
<td>Total</td>
<td>18/14.2</td>
</tr>
</tbody>
</table>

NCC: neurocysticercosis; TLE-HS: temporal lobe epilepsy associated with hippocampal sclerosis.

that consisted of mild renal insufficiency in one patient and a pulmonary embolus that was treated with anticoagulation in another. Both of these complications were resolved without further problems. There were no operative deaths.

DISCUSSION

NCC, an infection caused by the encysted larval stage of the tapeworm *T. solium*, constitutes one of the most common parasitic diseases of the nervous system in humans and is a major public health problem for most of the developing world. The clinical manifestations of NCC are variable and strongly depend on the number, type, size, location, and stage of development of the cysticerci, as well as the immune response of the host against the parasite.

Seizures are the most frequent manifestations of NCC (70-90%) followed by headache (38%), focal deficits (16%), and signs of intracranial hypertension (ICH, 12%). Other manifestations occur in fewer than 10% of symptomatic patients. Recent Brazilian investigations have reported that NCC seems to contribute to or even cause refractory epileptic discharges and may predict worst seizure outcomes in this group of patients. Bianchin et al. also noted that single NCC lesions are more commonly identified ipsilateral to HS, and this finding is suggestive of an anatomical relationship between TLE-HS and NCC.

CONCLUSIONS

The present study revealed that TLE-HS plus NCC is highly prevalent in patients with refractory epilepsy and that longer epilepsy duration and the involvement of multiple lobes may predict worst seizure outcomes in this group of patients. Early diagnosis and treatment may improve the prognoses of patients with TLE-HS plus NCC.

References


Lucas Crociati Meguins et al. Temporal lobe epilepsy and neurocysticercosis


