

Analysis of cerebrospinal fluid in racemose form of neurocysticercosis

Análise do líquido cefalorraquidiano na forma racemosa da neurocisticercose

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ABSTRACT

The present work aimed to evaluate the pattern of CSF alterations in patients diagnosed with neurocysticercosis (NCC) in racemose form. **Method:** This is a retrospective cohort study of patients with diagnosis of NCC in racemose form. CSF samples from 26 patients were analyzed. After patient-chart analysis was performed descriptive analysis of case studies and comparison between sexes in relation to variables were obtained with CSF by Mann-Whitney and Student's *t*-tests. **Results:** The sexes did not differ statistically when compared to pleocytosis in CSF. Eosinophils were present in 31% in samples while the ELISA test presented 80% sensitivity in this case series. Of the patient total, 24 presented a meningitis pattern with lymphocytic predominance. **Conclusion:** There was no difference in inflammatory pattern between the sexes, with predominance of lymphocytic meningitis and 80% sensitivity by ELISA test of CSF patients with racemose form of NCC.

Keywords: neurocysticercosis, racemose, cerebrospinal fluid.

RESUMO

O objetivo deste trabalho foi avaliar o padrão de alterações do LCR de pacientes com diagnóstico de neurocisticercose (NCC) na forma racemosa. **Método:** Trata-se de estudo de coorte retrospectiva, de pacientes com diagnóstico de forma racemosa da NCC. Foram analisadas amostras de LCR de 26 pacientes. Após análise de prontuário foi realizada análise descritiva da casuística e comparação entre sexos em relação às variáveis obtidas com o LCR por meio dos testes de Mann-Whitney e *t-Student*. **Resultados:** Não houve diferença estatisticamente significativa quando comparado à pleocitose no LCR entre os sexos. Houve presença de eosinofilia em 31% das amostras e o teste ELISA apresentou sensibilidade de 80% nesta casuística. Do total de paciente, 24 apresentaram padrão de meningite com predomínio linfocítico. **Conclusão:** Não houve diferença no padrão inflamatório entre os sexos, com predomínio de meningite linfocítica e sensibilidade de 80% ao teste ELISA do LCR de pacientes da forma racemosa de NCC.

Palavras-chave: neurocisticercose, racemosa, líquido cefalorraquidiano.

Neurocysticercosis (NCC) is an infection of the central nervous system caused by the larval form of the tapeworm *Taenia solium*, and is endemic in many low-income countries¹. The taeniasis-cysticercosis complex afflicts 50 million individuals in the world, of which 50 thousand die each year, estimating that approximately 400 thousand persons had the symptomatic disease in Latin America and that there is a much larger contingent of asymptomatic carriers^{2,3}. The majority of infected individuals belong to the age range between 20 and 50 years, resulting in large social and economic impact on the population⁴.

The form of presentation of the disease denominated cisternal or racemose, also known as the malignant form, is

often associated with intense inflammatory reaction in cerebrospinal fluid (CSF), chronic meningitis, arachnoiditis, thickening of the meninges of the base of the brain and can lead to a picture of blocked circulation of CSF with obstructive hydrocephaly and intracranial hypertension (ICH), with high mortality rates, varying from 20% to more than 50%^{5,6,7,8}.

Since CSF syndrome was described by Lange in 1940⁹, represented by the presence of pleocytosis, hyperconcentration of protein, eosinophils, there has been the development of immunological techniques, in recent decades, such as reactions of immunofluorescence, hemagglutination, immunoenzymatic test (ELISA-*enzyme-linked immunosorbent assay*) and *blotting* with purified glycoproteins (EITB-*enzyme-linked*

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immunotransfer blot), which provide higher CSF precision for establishing a diagnosis of cysticercosis^{10,11}.

Despite the epidemiological importance of NCC, especially in its racemose form, little has been described in the literature in relation to clinical findings or the characteristics of CSF in the Latin American population.

The present work aimed to evaluate the cerebrospinal fluid of patients diagnosed with the racemose form of NCC.

METHOD

This is a retrospective cohort study of patients with a diagnosis of racemose NCC, attended in the period from 1995 to 2010, in the Tropical Neurology Ambulatory Unit (ANTR) of HCFMRP-USP. The samples of cerebrospinal fluid from 26 patients were analyzed. A spinal tap indication was related to diagnostic support or a clinical criterion, in the majority of instances due to signals of probable meningitis.

The study was approved by the Committee for Ethics in Research and the participants signed Terms of Free and Informed Consent.

Statistical analysis

Descriptive analysis of case reports; comparison between the sexes in relation to the variables obtained with cerebrospinal fluid via the Mann-Whitney and Student's *t*-tests for independent samples. For data analysis, the software SPSS version 15.0 was utilized.

RESULTS

Data were evaluated from the charts of 26 patients with the racemose form of NCC presentation, totaling 100 samples of CSF exams analyzed. It was not possible to exclude from the CSF analysis the samples of patients using corticotherapy at the moment of collection for the exam due to the high percentage of patients under this type of treatment in the present study.

Of the 26 patients, 12 were females (46.1%) and 14 males (53.8%). The age of patients, at the moment of diagnosis, varied from 21 to 65 years, with a mean of 41 years.

The clinical presentations were intracranial hypertension (65.3%), epilepsy (53.8%), vasculitis of the central nervous system (3.8%) and arachnoiditis (30.7%). All the samples

presented abnormalities, characterizing this group as being carriers of meningitis. Topographies of racemose lesions were: 53.8% in basal cisterns, 88.4% in brainstem cisterns, 34.6% in Sylvian fissures, 42.3% in ventricles and 7.6% in spinal cord topography. One patient died during the study period.

The distribution of cellularity (pleocytosis) in CSF between the sexes is described in Table 1. None of the parameters analyzed showed a statistically significant difference in relation to sex.

All of the samples from twenty-four patients (92.3%) presented a pattern of meningitis with lymphocytic predominance. In the other two patients (7.7%) there was in some of their samples collected during the study period a predominance in the counting of eosinophils and/or neutrophils. The rate of cellularity, glucose and total protein are presented in Table 2.

As to the presence of eosinophil cells in the differential cellular count, among all the samples analyzed, this occurred in 31 samples (31%), whose distribution, according to the differential count percentages, is expressed in Table 3.

The ELISA immunological test for cysticercosis was performed on 95 CSF samples analyzed, of which 76 presented positivity, conferring a sensitivity of 80% to the test. The titers of the test were divided into one to 256, one to 1000 and one to 4000; the frequency of these distributions is represented in Table 4.

DISCUSSION

The CSF exam constitutes an important diagnostic and clinical tool in neurocysticercosis. The classical concept of CSF syndrome in NCC was introduced by Lange in 1940⁹, comprising the presence of eosinoflorraquia and positivity of the immunological exam. Our study has found eosinoflorraquia of 31% in CSF samples among the patients evaluated. Some works in the literature show that the presence of this cellularity pattern aids in the diagnosis of cysticercal meningitis, although its presence is unusual¹². The finding of eosinophil cells in the studied samples is probably an underestimate due to the widespread use of corticosteroids by the patients in our sample.

In the present study the predominant pattern of lymphocytic-type mononuclear pleocytosis (in 92.3% of the samples). This finding overlaps with other studies in the literature that evaluated CSF of NCC patients^{7,12,13}. The ELISA test is considered a lesser criterion

Table 1. Comparison between results obtained according to sex in relation to CSF variables.

CSF Variables	Female	p ¹	Male	p ¹	p
Cells	28.95 (7.8; 96.0)	< 0.0001	34.0 (17.0; 61.5)	0.001	0.647 ²
Glucose	42.3 ± 19.0	> 0.10	46.3 ± 20.9	> 0.10	0.317 ³
Protein	35.0 (19.5; 108.5)	0.012	49.8 (22.0; 118.0)	> 0.10	0.621 ²

1: Test of Shapiro-Wilk performed to evaluate normality of distribution of liquor variable values, by sex; 2: Test of Mann-Whitney for independent samples. Descriptive summary in median and quartiles; 3: Student's *t*-test for independent samples. Descriptive summary in mean and standard deviation.

Table 2. Rate of cells, glucose and protein in 100 CSF samples analyzed.

	Cells (mm ³)	Glucose (mg/dL)	Protein (mg/dL)
	%	%	%
0-20	37.2	14.4	24.7
20-40	16.7	31.9	24.7
> 40	46.1	53.7	50.6

Table 3. Rate of eosinophils in 100 CSF samples analyzed.

Eosinophils (%)	N	%
≤ 5	15	15.0
≤ 10 and > 5	9	9.0
≤ 30 and > 10	6	6.0
>30	1	1.0
Total	31	31.0

Table 4. Distribution of ELISA titers in CSF samples.

ELISA titers (N = 95)	N	%
≥ 1:4000	29	38.15
≥ 1:1000	12	15.78
≥ 1:256	13	0.50
< 1:256	20	26.32
Value not determined	2	2.63

in the NCC diagnostic panel, and presents approximately 87% sensitivity and 95% specificity in the literature¹⁴. The present study has shown a sensitivity of 80% for the test. In other works the sensitivities for the ELISA test varied from 62 to 87.5%, depending on the profile of the sample evaluated^{13,15,16,17,18,19,20}. Studies that specifically evaluated the sensitivity of the ELISA test in samples of

NCC patients in ventricular and cisternal topographies reported values from 93 to 100%^{12,15}. When evaluating the titer percentages of the ELISA test, the present study showed 38.1% of the titrations equal to or above 1/4000. A work by Minelli and Takayanagui found 21.4% for a similar titration²⁰.

The case series presented in this study did not confirm a statistical difference between the sexes as to the principal elements of CSF such as cellularity, proteins and CSF glucose; this finding stands in contrast to other studies that evidenced a greater inflammatory pattern in women²¹. Some studies report that the worst inflammatory pattern of CSF in women is related to a more exacerbated immunological response against the parasite, due to the levels of female steroids^{22,23,24,25}.

The Del Brutto diagnostic criteria do not apply to racemose form of neurocysticercosis through absence of scolex, and the diagnosis of these forms may be achieved with high sensibility and specificity only by CSF analysis.

The limitations of the study are related to sample size, the retrospective character of the data analysis, and the fact that the topographic data from the collections and pressure levels of CSF could not be analyzed on account of the great heterogeneity of topographies and lack of data in the medical charts. However, it is one of the few works in the literature that reports an analysis of cerebrospinal fluid in the racemose form of NCC, especially in a Latin American case sample.

Based on the findings of CSF in racemose NCC, there was a predominance of lymphocytic meningitis, sensitivity of 80% to the ELISA test but no difference in the inflammatory pattern between the sexes. However, these findings require greater clarification, with delineation of clinical trials, since many of these studies are experimental in character.

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