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Original

Cerebrospinal Fluid Changes in Experimental Model of Extraparenchymal Neurocysticercosis: preliminary results

Alterações no Líquido Cerebrospinal em Modelo Experimental de Neurocisticercose Extraparenquimatosa: resultados preliminares

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ABSTRACT

Introduction: *Neurocysticercosis (NCC) is the most common parasitic disease affecting the CNS and is considered a public health problem in many countries around the world, including Brazil. The cerebrospinal fluid (CSF) changes provoked by the disorder in humans are well defined in literature and were first described in 1940 by Lange. These modifications include pleocytosis, hyperproteinorrachia and eosinophilia. The majority of the experimental models of NCC published are focused on the parenchymal form of the disease. Few models studied the extraparenchymal form or analyzed the CSF parameters.* ***Objective:*** *To analyze the temporal modifications in the CSF of rabbits after the experimental induction of extraparenchymal NCC.* ***Method:*** *We included 14 male rabbits in this study. Each animal underwent a suboccipital injection of 50 cysts of T. crassiceps into the cisterna magna. Just before the inoculation, CSF samples were collected (sham). The animals were observed for 6 months, with monthly suboccipital punctures for CSF sample collection. Cellularity and protein concentration changes were analyzed throughout the observation period.* ***Results:*** *The initial cell counting average was only 1 (±0.88) cell/μL, raising to 1138.9 (±624.1) cells/μL in the first month and then dropping to 17.2 (±14.4) cells/μL in the sixth month. The differential analysis proved that, after the inoculation, lymphocytes were the most common cells in the CSF (85.1%, ±14.6). A similar pattern was identified with the proteinorrachia: an initial average of 25.8 (±8.3) mg/dL, increasing to 66.5 (±22.5) mg/dL one month later and then gradually decreasing to 40.2 (±15.6) mg/dL in the last month.* ***Conclusion:*** *It was possible to identify a substantial increase in cellularity and protein concentration in the CSF after the induction of NCC in rabbits, followed by a gradual fall over the remaining months. These variations are comparable to the findings in humans. The authors are currently giving continuity to this study, and stronger data will be released in future publications.*

Keywords: *Neurocysticercosis; Experimental models; Cerebrospinal fluid*

RESUMO

Introdução: *Neurocisticercose (NCC) é a doença parasitária mais comum do SNC e é considerada um problema de saúde pública em diversos países do mundo, incluindo o Brasil. As modificações no líquido cerebrospinal (LCR) provocadas pela doença em humanos estão bem definidas na literatura e foram inicialmente descritas em 1940 por Lange. Estas alterações incluem pleocitose, hiperproteinorraquia e eosinofilia. A maioria dos modelos experimentais de NCC publicados focam na forma parenquimatosa da doença. Poucos modelos estudaram a forma extraparenquimatosa ou analisaram os parâmetros de LCR.* ***Objetivo:*** *Analisar as modificações temporais no LCR de coelhos após a indução experimental de NCC extraparenquimatosa.* ***Método:*** *Foram incluídos 14 coelhos machos neste estudo. Cada animal recebeu injeção suboccipital de 50 cistos de T. crassiceps na cisterna magna. Imediatamente antes da inoculação, amostras de LCR foram coletadas (sham). Os animais foram observados por 6 meses, com punções suboccipitais mensais para colega de LCR. Modificações em celularidade e concentração proteica foram analisadas no período estudado.* ***Resultados:*** *A contagem média inicial de células foi de apenas 1 (±0,88) células/μL, aumentando para 1138,9 (±624,1) células/μL no primeiro mês e, então, caindo para 17,2 (±14,4) células/μL no sexto mês. A análise diferencial mostrou que, após a inoculação, linfócitos eram as células mais frequentes no LCR (85,1%, ±14,6). Um padrão similar foi identificado com a proteinorraquia: uma média inicial de 25,8 (±8,3) mg/dL, caindo para 66,5 (±22,5) mg/dL um mês após e, então, caindo gradualmente até 40,2 (±15,6) mg/dL no último mês.* ***Conclusão:*** *Foi possível identificar um aumento substancial na celularidade e concentração proteica do LCR de coelhos após a indução de NCC, seguido por uma queda gradual nos meses subsequentes. Estas variações são comparáveis aos achados em humanos. Os autores estão atualmente dando continuidade a este estudo, e dados de maior peso serão divulgados em futuras publicações.*

Palavras-chave: *Neurocisticercose; Modelos experimentais; Líquido cerebrospinal*

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Introduction

Neurocysticercosis (NCC) is the most common helminthic disease affecting the central nervous system (CNS)[1], and is considered a public health problem in many developing countries around the world, including Brazil[2]. The disease is caused by the cestode *Taenia solium*, when humans become its intermediate host after the ingestion of eggs of the adult tapeworm via fecal contamination[2,3]. The cerebrospinal fluid (CSF) changes associated with the disorder in humans are well defined in literature and were first described in 1940 by Lange[4]. These modifications include pleocytosis and hyperproteinorrachia.

Experimental models of NCC are important to help understanding the parasite-host interaction and the pathogenicity of the disease. The majority of the published experiments in NCC are focused on the parenchymal form of the disease. Few models study extraparenchymal NCC or analyze the CSF parameters[5,6,7].

The aim of this study was to analyze the temporal modifications in the CSF of rabbits after the experimental induction of extraparenchymal NCC via inoculation of *T. crassiceps cysts* into the subarachnoid space.

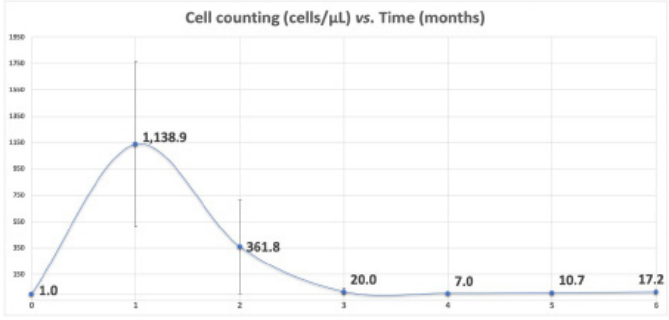
Method

We included 14 male rabbits in this study. The local ethics committee in animals research approved the proposed methodology. Each animal underwent a suboccipital injection of 50 viable cysts of *T. crassiceps* into the cisterna magna with a 22G needle. Just prior to the inoculation, CSF samples were collected (sham). The animals were observed for six months, with monthly suboccipital punctures for CSF sample collection. Cellularity and protein concentration changes were analyzed throughout the observation period. During this time, the animals were kept in individual cages (0.28m^2), with food and water *ad libitum*, in a climatized room.

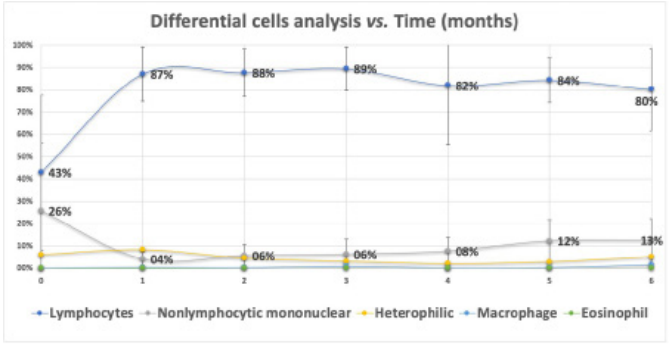
Results

The initial cell counting average before inoculation was only 1 (±0.88) cell/μL, leaping to 1138.9 (±624.1) cells/μL in the first month after the cysts injection and then gradually dropping during the following months (Graph 1)

The differential analysis proved that, after the inoculation, lymphocytes were the most common cells in the CSF (an average of 85.1%, ±14.6) (Graph 2).

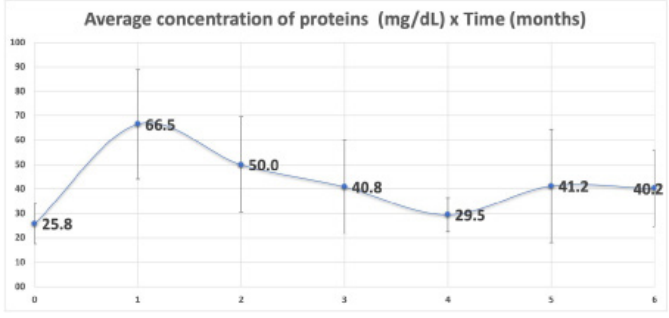


Graph 1. Cell counting averages fluctuations over the months.



Graph 2. Differential cells analysis: lymphocytic-type mononuclear predominance after inoculation.

A similar pattern was identified with the proteinorrachia: an initial average of 25.8 (±8.3) mg/dL, rapidly increasing to 66.5 (±22.5) mg/dL one month later, followed by a steady decrease (Graph 3).



Graph 3. Variations in concentration of protein over the months.

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Discussion

The CSF analysis is an important tool in the diagnosis and treatment of NCC in humans[3]. The most common findings in CSF of humans infected with *T. solium* include a lymphocytic-type mononuclear pleocytosis and high protein concentration in the CSF[8,9]. We observed the same pattern in our animals after the inoculation: cell counting average showed a sharp increase in the first month, and the proteinorrachia was over twice as high in the same time period as it was before the cysts injection. Also, the lymphocytes were the most common cells in the samples, similar to what is found in human NCC. Finally, the initial numbers were consistent to what is described in the literature as normal for healthy rabbits[10].

Conclusion

These preliminary results show that this model is feasible and can reproduce the findings in human NCC. The authors are currently giving continuity to this study, and further data shall be released in future publications.

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