

NEUROTOXOPLASMOSIS AND AIDS

CEREBROSPINAL, FLUID ANALYSIS IN 96 PATIENTS

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SUMMARY — The behavior of CSF inflammatory pattern in patients with AIDS and/or toxoplasmosis of the CNS is studied in 176 patients, divided in three groups. In the first group, 96 patients with toxoplasmosis and AIDS are considered; in the second group, 50 patients with toxoplasmosis without AIDS; in the third group, 30 AIDS patients without toxoplasmosis nor any other opportunistic infection. It is possible to conclude that patients with toxoplasmosis associated to AIDS exhibit CSF inflammatory pattern similar to patients with neurotoxoplasmosis without AIDS, except in respect to gamma globulin rates for which a cumulative effect can be detected.

KEY WORDS: toxoplasmosis, central nervous system, cerebrospinal fluid, acquired immunodeficiency syndrome.

Neurotoxoplasmose e AIDS: estudo do líquido cefalorraquiano em 96 pacientes

RESUMO — Foram estudados 176 pacientes com o objetivo de avaliar o comportamento da reação inflamatória no líquido cefalorraquiano (LCR) de pacientes com toxoplasmose do sistema nervoso central (SNC). Foram considerados três grupos de pacientes: o primeiro com toxoplasmose do SNC associada à síndrome de imunodeficiência adquirida (AIDS), com 96 pacientes; o segundo, com toxoplasmose, sem AIDS, com 50 pacientes; o terceiro, apenas com AIDS, sem qualquer infecção oportunista, com 30 pacientes. Verificou-se que o comportamento da reação inflamatória da toxoplasmose do SNC estudada pelo exame de LCR predomina sobre as características de base da AIDS, excepto no que diz respeito aos teores de globulinas gama; para estas, parece haver efeito cumulativo das duas patologias.

PALAVRAS-CHAVE: toxoplasmose, sistema nervoso central, líquido cefalorraquiano, síndrome de imunodeficiência adquirida.

Encephalitis or meningoencephalitis, usually related to immunodeficiency, characterizes the central nervous system (CNS) form of toxoplasmosis 5-7. There are foci of necrotic tissue in the brain, caused by the rupture of parasitic cysts, and nodules (granulomata), usually associated to cerebral edema, provided by host response to the presence of *Toxoplasma gondii* M.io. Many pathologies of the CNS may cause granulomata or necrotic foci, with clinical presentation similar to neurotoxoplasmosis. This can make the diagnosis sometimes very difficult 3. Neuroimage results are frequently unspecific 8,11. Serum immunological tests can provide information about the presence of specific antibodies. However, the worldwide prevalence of the disease is high, even without clinical manifestations. This can make the interpretation of serum immunological tests very problematic in a particular case 2,6,7,9.

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The present investigation aims to analyze main CSF inflammatory phenomena in patients with neurotoxoplasmosis, comparing a group with AIDS to another group without detectable immunodeficiency.

MATERIAL, AND METHOD'S

This study includes 176 patients with clinical symptoms suggestive of CNS infectious disease, submitted to CSF analysis. CSF inflammatory characteristics were present in all patients. These patients were divided in three groups.

In the first group were considered 96 patients with AIDS and neurotoxoplasmosis, without evidence of another associated infection. In this group, 79 (85%) were male, with male: female rate 5.7:1.0. Age ranged from 2 to 58 years, with mean \pm standard deviation $= 32.9 \pm 9.41$ years; median, 32.

The second group comprises 50 patients with neurotoxoplasmosis, without antibodies to HIV nor clinical manifestations suggestive of AIDS. In this group, 33 (66%) were male, with male: female proportion of 1.9:1.0. Age ranged from 1 day to 59 years; mean \pm standard deviation 19.4 ± 17.55 ; median 13.

The third group includes 30 patients with CSF inflammatory characteristics associated to HIV antibodies in the CSF, without evidence of infection by *Toxoplasma gondii* nor any other opportunistic detectable agent. In this group, 25 (83%) were male, with male: female rate 4.9:1.0. Age ranged from 24 to 65 years; mean \pm standard deviation 37.3 ± 10.99 ; median, 35.

CSF analysis was carried out in all patients. It includes: **classical examination** (at least cell count and cytomorphologic profile, proteins and protomogram, **glucose**, chlorides, enzymes); bacteriologic, mycologic and mycobacteriologic exams (direct and cultures); bacterial antigens (*Neisseria meningitidis* A, B, C, Y, W_{3,5}; *Hemophilus influenzae*; *Streptococcus pneumoniae*; *Streptococcus b*) and capsular antigens of *Cryptococcus neoformans* search; tests for detection of antibodies to syphilis, cysticercosis, schistosomiasis mansoni, Chagas disease, tuberculosis, histoplasmosis, paracoccidioidomycosis, candidiasis, aspergillosis; tests for antibodies to Cytomegalovirus, Varicella-zoster Herpes simplex and HIV.

In all patients were searched antibodies to *Toxoplasma gondii* in CSF: IgG antibodies by indirect immunofluorescence method and by passive hemagglutination test; IgM only by passive hemagglutination test.

CSF general inflammatory characteristics (cytology, proteins, gamma globulin) were considered for quantitative study. Hypotheses were analyzed by the Mann-Whitney U test ($\alpha = 0.10$).

RESULTS

Results for cells, proteins and gamma globulins in the CSF are summarized in Table 1.

Table 1. Cell count, proteins and gamma globulins of CSF.

Group	Variable	n	mean	SD	median	range
Toxoplasmosis + AIDS	cell count		53.1	171.15	3.7	0 - 1100
	proteins	96	90.9	94.73	59.1	17-520
	gamma globulins		21.5	7.10	20.1	8.0-40.9
Toxoplasmosis	cell count		24.6	71.21	7.0	0.3 - 380
	proteins	50	147.1	314.82	50.0	17-1800
	gamma globulins		15.5	8.13	13.0	8.0-50.8
AIDS	cell count		2.3	3.05	1.0	0.3 - 12
	proteins	30	47.6	11.18	50.5	20 - 65
	gamma globulins		17.9	6.97	15.8	9.5-37.0

n, number of patients; *SD*, standard deviation.

COMMENTS

In all cases, CSF possible interference factors must be considered: passive transference of systemic antibodies; blood-brain barrier breakdown in most patients with AIDS and/or other CNS diseases; low and inconstant titers of IgM and IgA in CNS chronic inflammatory diseases, even in exacerbation episodes^{2^}.

CNS images by computed tomography (CT) and magnetic nuclear resonance (MR) in patients with neurotoxoplasmosis are also unspecific. Many infectious and non-infectious diseases (CNS primary lymphoma, Kaposi sarcoma, neurotuberculosis, CNS mycoses, nocardiosis, brain abscesses) may exhibit similar CT and/or MR images. These are more important for follow-up after treatment than for specific diagnosis⁸⁻¹¹.

It is important to distinguish, in CSF examination, the actual inflammatory reaction related to the neurotoxoplasmosis and the isolated positivity of immunological reactions. The interaction between *Toxoplasma gondii* and host defense systems must elicit complex inflammatory phenomena, not isolated presence of specific antibodies. In some patients, this interaction does occur only in a sporadic way, due to the protection provided by granulomata i.3,4,io.

The neurotoxoplasmosis CSF inflammatory pattern in immunocompromised patients, particularly in AIDS, is not yet well established. The expression of inflammatory phenomena in patients with neurotoxoplasmosis associated to AIDS is different from neurotoxoplasmosis without AIDS? The answer to this question is very important to understand the difference between neurotoxoplasmosis and isolated positivity of immunological reactions, specially in a patient with AIDS.

In present investigation, there is a statistically significant difference between patients from group 3 (only AIDS) and patients from group 1 (toxoplasmosis and AIDS) related to cell count ($p = 0.001$), proteins ($p = 0.04$) and gamma globulins ($p = 0.004$). This means that occurrence of toxoplasmosis, as associated infection in patients with AIDS, modifies significantly the basal alterations related to AIDS.

The quality of this modification seems to be determined more by *Toxoplasma gondii* infection than by HIV infection. In fact, CSF inflammatory characteristics from patients with toxoplasmosis associated to AIDS (group 1) and CSF from patients with neurotoxoplasmosis without AIDS (group 2) are similar in respect to cell count ($p = 0.69$) and proteins ($p = 0.84$). However, gamma globulins rates are more elevated in patients with toxoplasmosis associated to AIDS ($p = 0.0009$); this may be explained by the basal high rates of gamma globulins present in patients with CNS involvement by AIDS.

In conclusion, patients with toxoplasmosis associated to AIDS exhibit CSF inflammatory profile similar to patients with neurotoxoplasmosis without AIDS, except in respect to gamma globulins rates; for these, a cumulative effect can be detected.

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