Arq Neuropsiquiatr 1995, 53(3-B): 604-607

HTLV-I ASSOCIATED TROPICAL SPASTIC PARAPARESIS

CEREBRAL SPINAL FLUID EVOLUTIVE ASPECTS IN 128 CASES

O.A. MORENO-CARVALHO, C.M.C. NASCIMENTO-CARVALHO**, B. GALVÃO-CASTRO****

SUMMARY- In order to evaluate if there is variation on the intensity of cerebral spinal fluid (CSF) response during HTLV-I associated tropical spastic paraparesis (TSP) evolution we retrospectively reviewed 128 cases.The results indicate that although CSF inflammatory alterations can persist over a 10-year period,they tend to become slight or even absent after the second year of TSP evolution.

KEY WORDS: tropical spastic paraparesis, cerebrospinal fluid, HTLV-I.

Paraparesia espástica tropical associada ao HTLV-I: aspectos evolutivos do líquido cefalorraqueano em 128 casos

RESUMO - Com o objetivo de verificar se existe mudança na intensidade da resposta inflamatória do líquido cefalorraqueano (LCR) no curso da paraparesia espastica tropical (PET) associada ao HTLV-I foram estudados retrospectivamente os exames de LCR de 128 pacientes com PET. Os resultados indicam que embora as alterações inflamatórias possam persistir por período superior a 10 anos, existe tendência a diminuição de sua intensidade ou mesmo de normalização após o segundo ano de evolução da doença.

PALAVRAS-CHAVE: paraparesia espástica tropical, líquido cefalorraqueano, HTLV-I.

An association between tropical spastic paraparesis (TSP) and HTLV-I has been described since 1985 in many parts of the world[2,4-8,10,12,14]. Autopsy histopathological data have shown that the inflammatory alterations of the spinal cord tend to become scarce or even absent in long term cases of TSP[1,9]. As cerebrospinal fluid (CSF) response is a reflection of the spinal cord and meningeal involvement and based upon the above mentioned information we decided to verify which are the evolutive aspects of CSF during HTLV-I associated TSP evolution.

MATERIAL AND METHODS

We retrospectively analyzed the CSF exams of HTLV-I associated TSP patients of our institution from November 1990 to October 1994. All of the patients complained of a variable period of weakness in their legs either associated or not with urinary and/or sexual disturbances. The diagnostic criteria used were a positive ELISA test for HTLV-I (HTLV-I EIA, Genetic System, Seattle, USA) plus confirmation by HTLV-I Western blot (Pageblot HTLV-I, Genetic System, Seattle, USA). All patients were also tested for syphilis, toxoplasmosis, schistosomiasis and cysticercosis antibodies by hemagglutination and immunofluorescent reactions. Regarding the patients, age, sex and period of evolution (Table 1) were analyzed and the CSF parameters considered were

*L.C.R., - Fundação José Silveira; **Federal University of Bahia; ***LASP-Fiocruz. Aceite: 30-abril-1995.

Dr. Otávio Augusto Moreno de Carvalho - L.C.R., Fundação José Silveira - Rua Bento Gonçalves s/n - 40140-000 Salvador BA - Brasil. FAX (071) 247 1590.

Table 1. Number of patients in each group according to the period of evolution, sex and age.

Period of evolution	Sex		Total	%
	Male	Female		
Group 1 (2mo-2ys)	16	27	**43**	(33.5)
Group 2 (2ys-5ys)	5	29	**34**	(25.5)
Group 3 (5ys-10ys)	9	**24**	**33**	(26.0)
Group 4 (> 10ys)	3	**15**	**18**	(14.0)
Total	33 (26.0%)	95 (74.0%)		-100
Age median and standard derivation	45 (25-66)	53 (24-70)		

Table 2. Mean (M) and standard deviation (SD) of the cell count and of the protein concentration in each group, according to the period of evolution.

CSF parameter	Period oof evolution							
	Group 1		Group 2		Group 3		Group 4	
	M	SD	M	SD	M	SD	M	SD
Cell count (WBC/mm^3)	22	19	13	9	12	9	9	9
Protein conc mg/dL	59	21	41	12	46	16	40	13

Table 3. Total number and its respective percentage of patients with CSF abnormal (A) and normal (N) parameters in each group.

CSF parameter	Period of evolution							
	Group 1		Group 2		Group 3		Group 4	
	A (%)	N (%)	A (%)	N (%)	A (%)	N (%)	A (%)	N (%)
Cell count	34(79)	9 (21)	28 (82)	6 (18)	25 (76)	8 (24)	14 (78)	4 (22)
Protein conc	35 (81)	8 (19)	15 (44)	19 (56)	16 (48)	17 (52)	6 (33)	2 (67)
Plasma cells*	29 (67)	14 (33)	20 (59)	14 (41)	16 (48)	17 (52)	2 (11)	16 (89)
Gamma globulin enhacement*	21 (51)	20 (49)	13 (39)	20 (61)	13 (43)	17 (57)	9 (50)	9 (50)

* Normal: absence of plasma cells and of gamma globulin enhancement.

cytology (cell/mm^3 count and cytomorphological profile), protein concentration (mg/dL), gamma globulin content (%) and presence of plasma cells (Tables 2 and 3).

The CSF exams were performed at the same laboratory and by the same person according to the same technique. For cell count (cells/mm^3) Fuchs-Rosenthal chambers were used; for cytomophological profile, accelerated gravitational sedimentation method and Leishman stain were proceeded; for protein concentration (mg/dL) the trichloride acetic acid method was used; for the gamma globulin content (%) electrophoresis on cellulose acetate was performed. It was considered only the first CSF exam of each patient and those that had negative reactions for syphilis, schistosomiasis, toxoplasmosis and cysticercosis.

The mean and the standard deviations of cell count and of the protein concentration of each group were compared by using Student *t* test[3]. To pleocytosis, hyperprotein concentration, presence of plasma cells and gamma globulin increase their percentage of occurrence was attributed and then its proportions were analyzed by using Fisher's exact test[3].

Table 4. Statistical analysis of the mean (m) and standard deviation (SD) of the cell count (cell/mm3) and of protein concentration (mg/dL) between the groups by using Student t test.

CSF parameter	Period of evolution		
	Group 1 x Group 2	Group 2 x Group 3	Group 3 x Group 4
Cell count	$0.01 < p < 0.02$	$0.60 < p < 0.70$	$0.20 < p < 0.30$
Protein conc	$p < 0.001$	$0.10 < p < 0.20$	$0.10 < p < 0.20$

Table 5. Comparison of CSF abnormal parameter proportions between the groups by using Fisher's exact test.

CSF parameter	Period of evolution		
	Group 1 x Group 2	Group 2 x Group 3	Group 3 x Group 4
Pleocytosis	$p = 0.21$	$p = 0.19$	$p = 0.26$
Hyperprotein	$p < 0.001$	$p = 0.27$	$p = 0.14$
Presence of plasma cells	$p = 0.14$	$p = 0.13$	$p < 0.01$
Gamma globulin enhancement	$p = 0.11$	$p = 0.19$	$p = 0.21$

RESULTS

One hundred fifty nine cases were reviewed and 128 were analyzed; 31 were not considered either because of lack of information about the period of evolution or because some of them had positive reactions for schistosomiasis.The patients were classified into four groups according to the period of evolution:Group 1, less than 2 years; Group 2, from 2 up to less than 5 years; Group 3,from 5 up to less than 10 years; Group 4, more than 10 years including 10 years.

Patient data are shown in Table 1. There is a significantly greater rate of CSF cell count and protein concentration in group 1 compared with group 2. The same does not occur when the other groups are compared (Table 4). A tendency to disappearence of plasma cells as time goes by was recorded and there is a significantly lower proportion of plasma cells in group 4 compared with group 3 (Table 5). Although there is a tendency for pleocytosis to become slight, that is not statistically significant (Table 5). There is a significantly greater proportion of hyperprotein concentration in group 1 compared with group 2 (Table 5). The proportions of gamma globulin enhancement were equivalent in the groups compared.

COMMENTS

CSF alterations in HTLV-I associated TSP patients have already been described[10,14], and they are characterized by moderate pleocytosis, moderate hyperprotein concentration, enhancement of gamma globulin, presence of plasma cells and eventually of eosinophils. Those surveys do not make a relationship between the data and the period of evolution, though. This survey shows that although CSF alterations can persist over a 10-year period, there is a tendency for that to become slight or even absent after the second year of disease. It suggests that there is a relationship between the autopsy findings[1,9] that show a lower degree of inflammation of the nervous tissue in long term patients and the CSF response in the course of HTLV-I associated TSP.

It is noteworthy that those patients who complain of more acute illness and refer to the disease as being progressive have a shorter period of evolution, whereas those with larger period of evolution usually refer to the disease as stopped or in slow progression. The mechanisms that unleash the disease are not fully understood but immunological activity seems to be important.It is likely that in some patients, once started, the complex mechanisms of the disease reach a peak in about a few

years and, then, tend to become slight or even stop with neurological sequelae.In other patients the mechanisms of the disease seem to perpetuate becoming less evident, though. Molecular research will come up with the answers about the intrinsic mechanisms of such a disease.

Acknowledgement - We thank the colleagues who sent their patients to our institution for cerebrospinal fluid exam, and Mr. Moilson Gonçalves for his technical assistance on HTLV-I ELISA and Western blot.

REFERENCES

1. Akizuki S, Nakazato O, Higuchi Y, Tanabe K, Setoguchi M, Yoshida S, Miyazaki Y, Yamamoto S, Sudou S, Sannomiya K, Okajima T. Necropsy findings in HTLV-I associated myelopathy. Lancet 1987, 1:156-157.
2. Araujo AQC, Alfonso CR, Schor D, Leite AC, Andrade-Serpa MJ. Clinical and demographic features of HTLV-I associated myelopathy/tropical spastic paraparesis (HAM/TSP) in Rio de Janeiro, Brazil. Acta Neurol Scand 1993, 88:59-62.
3. Berquó ES, Souza JMP, Gotlieb SLD. Bioestatstica. São Paulo: Editora Pedagógica e Universitária, 1980, p 205-222.
4. Cartier-Rovirosa L, Mora G, Araya F, Castilho J, Verdugo R, Miller MA, Gajdusek DC, Gibbs CJ Jr. HTLV-I positive spastic paraparesis in a temperate zone. Lancet 1989, 1:556-557.
5. Garruto RM, Yanagihara R, Asher DM. Seroepidemiologia del virus HTLV-I en el Pacifico occidental. In Zaninovic V(ed). Retrovirus Humanos: HTLV-I, paraparesia espastica y linfomas. Cali:Feriva Editores, 1989.
6. Gessain A, Vernant JC, Maurs L et al. Antibodies to human T-lynphotropic virus type-1 in patients with tropical spastic paraparesis. Lancet 1985, 2:407-410.
7. Janssen RS, Kaplan JE, Khabbaz RF et al. HTLV-I associated myelopathy/tropical spastic paraparesis in the United States. Neurology 1991, 41:1355-1357.
8. Melo A, Moura L, Rios S, Machado M, Costa G, Magnetic resonance imaging in HTLV-I associated myelopathy. Arq Neropsiquiatr 1993, 51:329-332.
9. Montgomery RD, Cruickshank EK, Robertson WB, Mcmenemey WH. Clinical and pathological observations on Jamaican neuropathy: a report on 206 cases. Brain 1964, 87:425-462.
10. Moreno-Carvalho OA, Santos JI, Di Credico G, Galvão-Castro B. Evidence of preferential female prevalence of HTLV-I associated tropical spastic paraparesis in Bahia, Brazil. Arq Neuropsiquiatr 1992, 50:183-188.
11. Roman GC, Spencer PS, Schoenberg BS, Madden DL, Sever JL, Hugon J, Ludolph A. Tropical spastic paraparesis in the Seychelles islands. Neurology 1987, 37:1323-1328.
12. Roman GC. The neuroepidemiology of tropical spastic paraparesis. Ann Neurol 1988, 23(Suppl):S113-S120.
13. Roman GC. Tropical spastic paraparesis and HTLV-I myelitis. In Vinken PJ, Bruyn GW, Klawans HL (eds). Handbook of clinical neurology, Vol 56.Amsterdam:Elsevier, 1989, p 525-542.
14. Spina-Franca A, Livramento JA, Machado LR, Gomes HR, Vianna LS, Castro LHM, Nobrega JPS, Bacheschi LA. HTLV-I antibodies in serum and cerebrospinal fluid in tropical spastic paraparesis in Brazil. Arq Neuropsiquiatr 1990, 48:441-447.
15. Vernant JC, Maurs L, Gessain A. HTLV-1 associated tropical spastic paraparesis in Martinique: a reappraisal. Ann Neurol 1988, 23(Suppl): S133-S135.