

CEREBROSPINAL FLUID IMMUNOGLOBULINS IN CYSTICERCOSIS OF THE CENTRAL NERVOUS SYSTEM

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Immunoglobulin G (IGG) is found in a higher proportion in the normal cerebrospinal fluid (CSF) than immunoglobulin A (IGA). Immunoglobulin M (IGM) has been found almost only in pathological conditions. In several different affections of the central nervous system (CNS) and/or its coverings which are accompanied by an increase of gamma globulin in the CSF protein profile — that characterizes the so-called chronic inflammatory profile — there also occurs a predominance of IGG over the other immunoglobulins. This predominance of IGG undergoes some fluctuations: many of them are proper to the disease considered, and other to its respective stage of evolution^{1, 2, 3, 6, 11}.

CSF changes proper to cysticercosis of the CNS⁵ are accompanied by changes in the protein profile that are proper to the chronic inflammatory type also. Data on the subject were first reported in 1960¹³ and were later confirmed by other investigations^{8, 9, 14}. However, no studies were reported with a view to establishing the behavior of CSF immunoglobulins in cases of cysticercosis.

This investigation aims at evaluating the behaviour of CSF globulins IGG, IGA and IGM in cases of cysticercosis of the CNS.

MATERIAL AND METHODS

Cases of cysticercosis of the CNS whose confirmed diagnoses were based upon the positive result of complement fixation test for cysticercosis (CFT) in the CSF were studied. None of the patients had undergone neurosurgical manipulation prior to this investigation. Two series of cases are comprised in this study, the first one composed of 30 CSF samples, and the second of 5.

In the first series (cases 1 to 30) the CSF samples were studied as to: titer of positive CFT; total protein concentration; electrophoretic profile of proteins; agar-

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diffusion against immunoserum for IGA, IGM and IGG, first without concentration of sample and then after a 10-time previous concentration; IGA, IGM and IGG concentration. In the second series (cases 31 to 35) it was established the relative proportion of IGA, IGM and IGG, starting from the concentration values found in CSF samples concentrated around 100 times.

The titer of positive CFT was established according to the Kolmer technique⁴; results were expressed in units. Total protein concentration was determined through the trichloroacetic acid method according to standardization previously reported¹⁵. The protein profile was analyzed through electrophoresis, and according to the technique previously reported¹²; previous concentration of CSF sample was carried out through dialysis against gum arabic; cellulose acetate gel strips (Cellogel, Chemetron) were employed. Concentrations of albumin fraction and gamma globulin fraction were calculated considering their relative proportion in the protein profile and the total protein concentration of the CSF sample.

Agardiffusion was carried out according to Ouchterlony technique¹⁰: 20 microliters of the sample and 20 microliters of immunoserum anti IGA, IGM or IGG, produced in rabbits (Behringwerke), were used; results are expressed with a plus (+) sign when precipitation line was evidenced, and with a minus (-) sign when not-evidenced.

IGA, IGM and IGG concentrations were evaluated through radial immunodiffusion technique according to Mancini⁷, and Behringwerke immunoplates were used: LC-type in the first series, using 20 microliters of each CSF sample, and 20 microliters of three different dilutions of standard serum (Behringwerke); Tripartigen-type in the second series, using 5 microliters of each CSF sample concentrated around 100 times, and 5 microliters of three different dilutions of the standard serum already mentioned. With base on the results obtained for the standard serum, it was calculated the concentration of each immunoglobulin in the samples of CSF which were tested. For the second series, the proportion of IGA, IGM and IGG was established, with base on the concentration found for each one of them.

For the first series, it was calculated the correlation (r) between: CFT titer and albumin concentration; CFT titer and gamma globulin concentration; CFT titer and IGG concentration; gamma globulin concentration and IGG concentration. Differences between correlation values were calculated for $z(r)$ of Fisher and through Student's t test; significance was evaluated according to Snedecor's table.

RESULTS

For the 30 cases of first series, results referring to titer of positive CFT, concentrations of total proteins, albumin, gamma globulin, IGA, IGM and IGG are presented in table 1. Evidence of IGA, IGM and IGG through agardiffusion for non-concentrated CSF samples and for 10-time concentrated samples is presented in table 1, also.

Table 2 shows the relative concentrations found for IGA, IGM and IGG for samples of the second series (5 cases), which were concentrated around 100 times. Analyzed correlation values are shown in table 3.

COMMENTS

Investigations on the increase of gamma globulin in the CSF in cases of cysticercosis of the CNS already mentioned¹³ showed that there is a positive correlation between the concentration of gamma globulin in the CSF and the respective titer of positive CFT. Data gathered in the present investigation support these findings since, for the first series of cases, it was found also a positive correlation between these data ($r = 0.60$; $P < 0.01$).

Case	CFT	Total pro- tein	Al- bu- min	Gam- ma glob.	IGA	IGM	IGG	Unconcentrated CSF			Concentrated CSF		
								IGA	IGM	IGG	IGA	IGM	IGG
1	1	34	23.1	3.0	0.9		3.5	-	-	+			
2	2	32	17.0	6.2			6.2	-	-	+			
3	8	34	20.7	5.2			8.0	-	-	+			
4	2	34	21.1	4.7			4.6	-	-	+			
5	2	36	20.2	5.0		1.6	2.2	-	-	+			
6	32	48	19.7	11.3			7.3	-	-	+	-	-	+
7	64	56	25.2	15.7			12.2	-	-	+			
8	4	39					5.6	-	-	+			
9	8	53	31.3	8.6			2.2	-	-	+	-	+	+
10	2	38					2.4	-	-	+			
11	2	25	13.7	6.1			5.7	-	-	+	-	-	+
12	8	25	14.0	4.9			4.9	-	-	+			
13	4	49	28.9	10.5			10.4	-	-	+	+	-	+
14	16	31	14.6	8.7			8.2	-	-	+	+	-	+
15	4	38	16.7	10.1			4.3	-	-	+			
16	4	42	21.8	12.0			12.0	-	-	+	+	-	+
17	1	19					2.2	-	-	+	+	-	+
18	2	36					5.0	-	-	+			
19	2	29					8.4	-	-	+	-	-	+
20	2	42	19.7	10.4			15.2	-	-	+	+	-	+
21	4	47	27.7	6.9			6.6	-	-	+	+	-	+
22	1	39	19.1	4.2			2.9	-	-	+	-	-	+
23	32	38	18.6	6.5			6.5	-	-	+			
24	8	26	11.4	3.9		2.2	8.8	-	-	+	+	-	+
25	4	58	24.4	16.1			6.6	-	-	+	+	-	+
26	2	29	14.5	7.2		2.0	6.1	-	-	+	-	+	+
27	64	36	20.5	6.9			8.8	-	-	+			
28	1	36	21.6	4.8			5.0	-	-	+			
29	1	16	9.0	2.2			1.7	-	-	+	-	-	+
30	1	29	15.7	2.9			2.0	-	-	+	-	-	+

Table 1 — Cerebrospinal fluid data in cystercosis of central nervous system: cases of the first series. CFT, titer of positive complement fixation test for cystercosis. Total protein, albumin, gamma globulin, IGA, IGM, IGG: concentrations in mgm/100 ml. Agardiffusion of unconcentrated and 10-time concentrated CSF samples against IGA, IGM and IGG immune antiserum: results expressed with a plus (+) sign when precipitation line was evidenced, and with a minus (-) sign when not-evidenced.

A positive correlation between CFT titer and IGG concentration was also clear ($r = 0.40$; $P < 0.05$). The difference between its value and the value found for correlation of concentration of gamma globulin and titer of CFT was not significant ($t = 0.93$; $P > 0.05$). As a counterproof it was calculated the correlation between this same titer and the albumin fraction concentration: the values found were not significant ($r = 0.13$; $P > 0.05$) and this demonstrates that there is no correlation between the two of them, as it was expected.

Presence of IGG was a constant, as can be seen in data referring to the first series of cases; in the average (6.2 mgm/100 ml) it proved to be superior to normal values reported in literature^{6,11}. In this same series

IGG represented an average of 16.1% of total protein concentration; gamma globulin concentration represented an average of 20.1% of the total protein concentration. IGG concentration represented also an average of 87.9% of the gamma globulin concentration. There was a significant positive correlation between the representative values of IGG concentration and gamma globulin concentration ($r = 0.67$; $P < 0.01$).

IGA and IGM were present, in the first series of samples of the cases analyzed, as follows: in none of the cases when agar diffusion of non-concentrated CSF was considered; IGA in one sample and IGM in three samples, when radial immunodiffusion was considered. However, when 10-time concentrated CSF samples were used — and it was possible to do that in 16 of the cases — IGA was found to be present in 8 cases, and IGM in 2.

Ten-time concentrations, though low, were enough to show these other immunoglobulins in a higher proportion of the samples than when samples not previously concentrated are used. This fact shows that it is necessary to concentrate the sample satisfactorily for an adequate study of these fractions which usually occur in the CSF in a much lower concentration than that of IGG. The concept of "satisfactory", in this case, implies concentrating the sample up to levels close to those which are characteristic of total protein concentration of blood sera. It was with a base on this principle that it was made the analyses of the second series of 5 cases, in which each one of the samples was concentrated around 100 times.

Case	IGA (%)	IGM (%)	IGG (%)
31	15.2	13.4	71.4
32	22.4	8.5	69.1
33	13.2	5.8	81.0
34	0.0	0.0	100.0
35	8.6	10.7	80.7

Table 2 — Cerebrospinal fluid data in cysticercosis in the cases of the second series. Relative concentration of IGA, IGM and IGG established through radial immunodiffusion in CSF samples concentrated around 100 times.

Correlation	r
CFT and gamma globulin concentration	0.60
CFT and IGG concentration	0.40
CFT and albumin concentration	0.13
Gamma globulin and IGG concentrations	0.67

Table 3 — Correlations (r) analyzed for data pertinent to CSF samples of the first series of cases. CFT, titer of positive complement fixation test for cysticercosis.

Through analysis of this latter series it can be verified that, with the exception of one case, presence of the three immunoglobulins studied can be demonstrated; a higher proportion of IGG (80.4, average) is confirmed in relation to IGA and IGM (11.9% and 7.7% average, respectively).

These data prove that for an appropriate study of events characteristic of IGA and IGM, in inflammatory processes which produce immunobiological modifications in the CSF similar to those found in cysticercosis of the CNS, it is necessary to use properly concentrated samples or more precise methods than those currently available — and hereby analyzed.

Data obtained as to IGG show it to be the main immunoglobulin occurring in the CSF in cases of cysticercosis of the CNS. In such cases, it is part of the protein profile in a proportion higher than the usually referred in normal CSF. In this series, this proportion was of 16%, representing about 88% of the gamma globulin concentration. There is an unmistakable correlation between gamma globulin concentration and IGG concentration — and also between the latter and the CFT positivity titer.

SUMMARY

Investigation on the behavior of immunoglobulins IGG, IGA and IGM in the CSF in cases of cysticercosis of the CNS, based on data pertaining to two different series of cases. The first series comprises 30 samples of CSF, and the second one, 5 samples. It was demonstrated that IGG is the one representing the largest contingent. IGG concentration keeps in proportion with the gamma globulin concentration, of which it represented an 88% average in the cases studied. Participation of IGG in the protein profile of the CSF is greater than the usually referred; the results for the material analyzed showed 16%. It was verified a proportionality also between IGG concentration and the titer of positive complement fixation test for cysticercosis; there is a positive correlation, whose numerical expression was found to be significant in the samples studied.

RESUMO

Imunoglobulinas do líquido cefalorraqueano na cisticercose do sistema nervoso central

Investigação sobre o comportamento das imunoglobulinas IGG, IGA e IGM no líquido cefalorraqueano (LCR) na cisticercose do sistema nervoso central baseada em dados pertinentes a duas séries de casos. A primeira compreende 30 amostras de LCR e, a segunda, 5. Foi verificado que a IGG representa o maior contingente das imunoglobulinas estudadas. A concentração de IGG guarda proporção com a de gama globulina, de que repre-

sentou 88% em média. A participação de IGG no perfil proteico do LCR é maior do que o habitualmente referido, sendo de 16% para o material analisado. Foi verificado também haver proporcionalidade entre a concentração de IGG e o título da positividade da reação de fixação do complemento para cisticercose: há correlação positiva, cuja expressão numérica foi significativa para as amostras estudadas.

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