SERUM ANTIBODIES AGAINST SOME VIRUSES IN SCHIZOPHRENIA PATIENTS

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Key-words: schizophrenia — serum antibodies — herpes simplex virus type I, II — cytomegalovirus — influenza viruses

Certain investigators suppose that some slow or latent virus infections are related to the development of mental changes (7, 11, 13). It is known that diseases caused by viruses of the herpes group can induce psychotic status and that relapsing herpes simplex labialis often occurs in psychoses in the young age (5, 8, 12). More concretely, in schizophrenia most clinical and epidemiological aspects of the disease enable the presumption of an etiological relation with an infectious viral agent (4, 6). T. Crow (1978), R. Rimon (1983) a. oth. report the presence of high titres of serum antibodies against herpes simplex virus in schizophrenia patients. D. Tyrell et al. (1978) isolate virus-like agents from the cerebrospinal fluid of such patients causing cytopathogenic effect on cell cultures.

On the grounds of these and some other similar communications published recently we decided to study the humoral immune response against some virus agents in schizophrenia patients (7).

Material and methods

We investigated a total of 38 patients (23 females and 15 males) aged between 15 and 52 years (mean age 31 years) treated in the Psychiatric Clinic of the Higher Institute of Medicine, Varna during the period 1983—1984. Patients' diagnosis was schizophrenia, predominantly paranoid form, with paroxysmal-progredient course and no more than three attacks of the illness. Blood tests were taken during the first days of hospitalization (concerning the first serum trial) and before discharge from hospital (concerning the second one). Somatically healthy persons were selected for investigation. The control group consisted of a total of 40 healthy blood donors aged between 20 and 40 years (mean age 33 years) participating in the examination with a single blood test only.

We determined the level of serum complement-binding antibodies by using of CFT after Dobrev (2). A set of herpes antigens type I and II as well as cytomegalovirus was applied. We used 5 influenza virus diagnostic strains (presented on table 3) applied in the recent years for collective influenza immunity determination in Bulgaria, as control antigens in our study. We assessed the hemaglutination antibody levels by using of IHT in the same patients. All the diagnostica and bioproducts used in our investigation were given up to us by the Research Institute for Infectious and Parasitic Diseases of the Medical Academy in Sofia. Statistical data processing was carried out after the method of variation analysis by using of the microprocessor system IZOT-1002-C which was at disposal in the Higher Institute of Medicine, Varna.

Results and discussion

The results obtained were shown on tables. On table 1 one could see the data from the statistical processing of mean geometrical titres (MGT) of complement-binding antibodies against herpes antigens and cytomegalovirus (CMV) in double serum samples from schizophrenia patients. There was a statistically significant difference between the first and second serum tests of MGT against herpes simplex virus (HSV), type I ($p < 0.001$). However, complement-binding antibody increase in the second serum test against HSV, type II was statistically insignificant despite of the different results concerning MGT (2.69 for the first and 2.83 for the second serum) ($p > 0.05$). It was obvious that the lowest MGT were obtained when CMV was concerned (2.47 for the first and 2.75 for the second serum). However, antibody enhancement in the course of the disease was statistically significant ($p < 0.001$). Table 2 reflected the results from the comparison of the data of patients and controls. It was evident that MGT of complement-binding antibodies in schizophrenia patients surpassed these of healthy individuals. There were reliable differences between the level of antiherpes antibodies from the first and the second serum tests of patients and control sera concerning both HSV types ($p < 0.001$). However, the comparison of MGT against CMV revealed insignificant differences between schizophrenia patients and healthy controls ($p > 0.1$ concerning the first serum test and $p > 0.05$ concerning the second one). It could be concluded that there was a more active complement-binding antibody production against HSV type I and II in schizophrenia patients as compared with that of healthy individuals.

Table 1

Comparison of mean geometric titres of complement-binding antibodies towards VHS type 1 and 2 and cytomegalovirus in double serum samples* from schizophrenia patients

Studied antibodies towards	MGT	Statistical indexes				
		$\bar{x}$	S	m^2	t	p
VHS type 1 1^{st} serum	8.0	3.03	0.3958	0.0043	4.46	<0.001
VHS type 1 2^{nd} serum	9.8	3.28	0.1970	0.0011		
VHS type 2 1^{st} serum	6.5	2.69	0.2306	0.0016	1.73	>0.05
VHS type 2 2^{nd} serum	7.0	2.83	0.5422	0.0082		
Cytomegalovirus 1^{st} serum	5.7	2.47	0.2394	0.0016	12.5	<0.001
Cytomegalovirus 2^{nd} serum	6.5	2.75	0.3608	0.0001		

* n sera = 36

Table 2

Comparison of mean geometric titres of complement-binding antibodies towards VHS type 1 and 2 and cytomegalovirus in sera from schizophrenia patients and healthy individuals

Studied antibodies towards	Schizophrenia patients				Healthy controls					
	MGT	$\bar{x}$	S	m^2	MGT	$\bar{x}$	S	m^2	t	p
VHS type 1 1st serum	8.0	30.3	0.3958	0.0043	4.3	2.1	1.685	0.071	3.39	<0.001
VHS type 1 2nd serum	9.8	3.28	0.1970	0.0011					4.39	<0.001
VHS type 2 1st serum	6.5	2.69	0.2306	0.0016	2.0	0.93	1.29	0.0416	8.46	<0.001
VHS type 2 2nd serum	7.0	2.83	0.5422	0.0082					8.52	<0.001
Cytomegalovirus 1st serum	5.7	2.47	0.2394	0.0016	5.7	2.50	1.378	0.0475	0.136	>0.10
Cytomegalovirus 2nd serum	6.5	2.75	0.3608	0.0001					1.15	>0.05

In order to establish the kind of humoral immune response in relation to another antibody type (in this case — hemagglutination ones) in the same patients' contingent we investigated the double serum tests towards 5 influenza virus types. These results were demonstrated on table 3. We could not establish any significant MGT increase of the hemagglutination antibodies in the second serum test of the patients against 4 from all 5 influenza diagnostica ($p>0.10$). Type A — Hong-Kong, 1/68 (H_3N_2) was an exception. Its variants recently circulated and could, therefore, stimulate a synthesis of antibodies specific to «forefather». However, when compared separately, MGT of hemagglutination antibodies in the first and second serum test of patients differed statistically significantly from these of healthy individuals assessed concerning their collective antiinfluenza immunity against the same virus types in 1984 ($p<0.001$).

We could draw a general conclusion from the results obtained that in schizophrenia patients studied which were at the active age and somatically healthy during the progress of active psychotic manifestations an active humoral immune response against certain antigens from virus origin could be established. In another unpublished study (3) we found out reliably higher serum immunoglobulin G, A and M levels in patients with the same disease as compared with these of healthy persons. According to M. E. Vartanyan (1976), the presence of high serum immunoglobulin levels in schizophrenia patients argued for an immunological reorganization of their organism. Probably, such an immunological reorganization was considered in this case but it was difficultly to clarify the reason for plasma protein stimulation in schizophrenics at this stage of knowledge. H. Libikova et al. (1978) and other investigators asserted that this problem in schizophrenia could be concretely solved by application of complex genetic, virologic, biochemical, cell-molecular and physiological investigations.

Table 3

Comparison of mean geometric titres of hemagglutination antibodies towards influenza antigens in double serum samples from schizophrenia patients and healthy individuals

Influenza diagnostica/ MGT in healthy	MGT in patients		f_1 *	p_1	t_2	p_2	t_3	p_3
A-USSR — 90/70	1st ser.	79.43	1.32	>0.10	14.16	<0.001	12.3	<0.001
MGT=16.79	2nd ser.	98.99						
A-Hong Kong-68	1st ser.	27.84	20.0	<0.001	5.91	<0.001	21,1	<0.001
MGT=50.09	2nd ser.	273.4						
A-Bangkok-1/79	1st ser.	144.7	0.57	>0.10	5·32	<0.001	6.7	<0.001
MGT=63.16	2nd ser.	158,5						
A — Texas — 1/77	1st ser.	183.3	1.59	>0.10	8.1	<0.001	12.4	<0.001
MGT=67.26	2nd ser.	232.0						
B-Singapore 222/79	1st ser.	13.87	1.3	>0.10	10.6	<0.001	7.21	<0.001
MGT=32.20	2nd ser.	15.75						

* Statistical indexes when comparing MGT between:
t_1, p_1 — first and second serum from schizophrenia patients
t_2, p_2 — first serum from patients and serum from controls
t_2, p_2 — second serum from patients and serum from controls

On the basis of the aforementioned data the following conclusions could be made:

1. There is a significant increase of complement-binding antibody titres in the second serum test of schizophrenics against HSV type I and CMV.

2. Antiherpes antibody levels against HSV type I and II in sera of schizophrenics are reliably higher than these of healthy individuals.

3. A more active hemagglutination antibody production against various influenza virus types in the same patients as compared with that of healthy controls.

REFERENCES

1. Вартаньян, М. Е. В: Шизофрения. Киев, Здоровья, 1976, 22—24. — 2. Добрев, И. *Лет. ХЕС;* 1976, № 3, 141—151. — 3. Евтимова, В. Непубликувани данни. — 4. Albrecht, P., E. Boone, E. Torrey, J. Hicks. *Lancet*, 2, 1980, 769—772. — 5. Crow, T. J. *Postgrad. Med. J.*, 54, 1978, No 637, 763—767. — 6. Crow, T. J. *Lancet*, 1, 1983, No 8317, 173—175. — 7. Gotlieb-Stematsky, T., J. Zonis, A. Arlazoroh, T. Mozes, M. Sigal, A. Szekely. *Arch. Virol.*, 67., 1981, 333—339. — 8. Hanshaw, J. B., A. P. Scheiner. *New Engl. J. Med.* 295, 1976, 468—471. — 9. Ivanova, L., et al. *Scr. sci med.*, 14, 1978, 83—92. — 10. Libikova, H., J. Pogady, J. Rajcani, J. Skodacek, F. Ciampor, M. Kocisova. *Acta Virol.*, 23, 1979, 231—239. — 11. Rimon, R. *Ann. Clin. Res.*, 15, 1983, No 1, 1—3. — 12. Shearer, M. L., S. M. Finch. *New Engl. J. Med.*, 271, 1964, 494—497 — 13. Tyrell, D. A., T. J. Crow, R. P. Parry, E. Johnstone. *Lancet*, 1, 1979, 839—841.