CHANGED IMMUNOLOGICAL BRAIN PROTEIN SPECIFICITY IN ACUTE TRAUMATIC EDEMA AND EDEMATOUS SWELLING OF "TUMOR ORIGIN"

(UDC 616.831-005.98-02:/616.831-001-616.831-006/-092.4/.9-07:616.831-008.939.6-07)

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Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 57, No. 5, pp. 36-39, May, 1964
Original article submitted February 7, 1963

The causes for the occurrence and development of edematous swelling of the brain have been inadequately studied. The numerous biochemical, morphological, and physiological investigations [5, 11], 12] did not present sufficiently convincing data which would permit us to elicit the genesis of this complex pathological process. In our earlier experiments [1, 3, 4] with the use of labeled amino acids, iodized serum proteins, inorganic radiophosphorus compounds, and radioiodine, we investigated certain aspects of the mechanism of the pathogenesis of experimentally induced acute traumatic edema of the brain. It was established that in the given pathological process complex metabolic disorders occur in the brain which change the physico-colloidal state of the brain tissue and the physiological properties of the tissue-blood barriers. However, there are no studies on the role of structural changes of brain proteins in the development of edematous swelling of brain tissue. Here we are interested in an investigation of the immunological specificity of brain proteins in edema (appearance of autoantigens) since the biological properties of proteins are conditioned by their labile tertiary structure.

It is known that autoantigens appear as the result of the formation of complexes of "normal" tissue proteins with various substances, in the presence of some degree of denaturation of the proteins of the body (cold, trauma, burns, etc.), in disorders of certain enzyme systems, entrance into the blood of products that are not broken down, etc. [10]. It was established for nervous tissue that autoantigens arise as a result of its trauma and in various neuropsychic diseases [8].

We investigated the changes in the immunological specificity of brain proteins arising in its acute traumatic edema and edematous swelling around the growing brain tumor.

METHOD

Acute traumatic edema of the brain was induced in rats by Klosovskii's method [7]. A transplantable rat brain tumor was obtained at the Uzbek Scientific Research Institute of Roentgenology, Radiology, and Oncology [2].

The immunological specificity of the proteins from the zone of acute traumatic edema of the brain was investigated 30 min after its occurrence, and from the edema zone around the brain tumor at the terminal stage of the disease. In the animals with traumatic edema and in the group of rats with the transplantable tumor we simultaneously isolated the proteins from the opposite hemisphere and from the tumor itself (the immunological specificity of proteins from a tumor was established in our previous investigations [9]).

The antigen was obtained by the method of Zil'ber and team [6].

So that the results of the experiments would not be affected by individual differences in the immunological specificity of the brain proteins of the experimental animals, the antigen was prepared simultaneously (from 15 rats in each series of experiments) for all experiments.

TABLE 1. Anaphylactic Reaction with Desensibilization in the Investigation of Proteins Isolated from the Zone of Acute Traumatic Brain Edema of Rats

No. of guinea pigs	Sensibilization		Desensibilization by a mixture of "normal" antigen and erythrocytes						Resolving injection	
	Antigen from zone of traumatic brain edema (in mg)	Reaction	First injection (in mg)	Reaction	Second injection (in mg)	Reaction	Third injection (in mg)	Reaction	Antigen from zone of traumatic brain edema (in mg)	Reaction
1	3,2	—	18	++	6	+	8	—	7	++
2	3,2	—	18	++	6	+	8	—	7	++
3	3,2	—	18	+	6	—	—	—	7	+++
4	3,2	—	18	+	6	—	—	—	7	+
5	3,2	—	18	—	6	—	—	—	7	+
6	3,2	—	18	—	6	—	—	—	7	+
7	4,5	—	18	—	6	—	—	—	7	±
8	4,5	—	18	—	6	—	—	—	12	+

Annotation. Here and henceforth the key is as follows: +++ severe form of anaphylactic shock, ++ anaphylactic shock of average severity, + mild form of anaphylactic shock, ± doubtful reaction.

The immunological specificity of the isolated proteins was studied by the method of anaphylaxis with desensibilization on guinea pigs.

In the I series of experiments we used antigen from the zone of traumatic brain edema for sensibilization and the resolving injection, and for desensibilization antigen from the opposite hemisphere of the brain of the same animals.

The guinea pigs were sensibilized by a single injection of 3.2-4.5 mg of antigen subcutaneously. Nineteen to twenty days after injecting the animals, we counted those sensibilized. Desensibilization was accomplished by a subcutaneous injection of a mixture of "normal" antigen and a suspension of erythrocytes in a quantity of 18 mg 18-20 h before the resolving injection. The erythrocytes were used to preclude the effect of a possible presence of blood in the edematous tissue on the anaphylactic reaction. To verify the completeness of desensibilization, the indicated antigen was reinjected intravenously in a dose of 6 and 8 mg until a negative anaphylactic reaction to the injection was obtained.

Anaphylactic shock was induced by an intravenous injection of a solution of the test antigen in a quantity of 7-12 mg.

In the II series of experiments we used protein isolated from the zone of edematous swelling around the brain tumor for sensibilization and the resolving injection. Desensibilization was accomplished by a mixture of proteins

TABLE 2. Anaphylactic Reaction with Desensibilization in Investigation of Proteins Isolated from the Zone of Edema Around the Brain Tumor of Rats

No. of guinea pigs	Sensibilization		Desensibilization by a mixture of "normal" and tumor antigens and erythrocytes						Resolving injection	
	Antigen from zone around tumor (in mg)	Reaction	First injection (in mg)	Reaction	Second injection (in mg)	Reaction	Third injection (in mg)	Reaction	Antigen from zone around tumor (in mg)	Reaction
1	3,2	—	18	+	6	+	8	—	7	+
2	3,2	—	18	—	6	—	—	—	7	—
3	3,2	—	18	—	6	—	—	—	7	—
4	3,2	—	18	—	6	—	—	—	12	±
5	3,2	—	18	—	6	—	—	—	12	++
6	3,2	—	18	—	6	—	—	—	12	—
7	3,2	—	18	—	6	—	—	—	12	—
8	3,2	—	18	—	6	—	—	—	12	—

obtained from healthy brain tissue and the brain tumor and erythrocytes. The method of verifying the anaphylactic reaction with desensibilization in this series of experiments was the same as the preceding.

Anaphylactic shock was evaluated by the behavior of the animals and the degree of body temperature drop.

RESULTS

We see from Table 1 that out of 8 animals 1 developed a severe form of anaphylactic shock, 2 average, 4 mild appearances of shock, and in 1 the reaction was doubtful. Consequently, the immunological specificity of proteins is changed in acute traumatic edema of the brain, which indicates a deep disturbance of their structure.

In most cases, it was not possible to establish changes of the antigenic structure of the brain proteins in the zone of edematous swelling around the implanted tumor (Table 2). Anaphylactic shock of a mild and average form was established in two observations out of eight. Apparently, in these cases the change in the immunological specificity of the proteins of the brain tissue around the tumor were caused by the toxic effect of the decomposition products of the tumor itself on the surrounding tissue.

Thus, in the occurrence of acute traumatic edema of the brain gross changes in the structure of brain proteins occur in the affected areas of brain tissue (on investigation as early as 30 min after its occurrence); such changes were not detected in edematous swelling around the growing tumor. These data confirm our previously expressed (on the basis of complex radiometric investigations) hypotheses on the different mechanism of occurrence of acute traumatic brain edema and edematous swelling of a tumor origin.

SUMMARY

The work concerns the changes in immunological specificity of brain proteins in rats with acute traumatic edema and edematous-swelling around the growing cerebral tumor.

Immunological specificity of proteins from the traumatic edema zone of the brain was studied 30 min after its onset from the edema zone around the brain tumor and at the terminal stage of the disease (by the method of anaphylaxis with desensitization).

As established, in acute traumatic brain edema there occur changes of immunological specificity of the proteins, indicating a profound disturbance of their structure. In the greater proportion of the cases it was impossible to detect any changes in the antigenic structure of cerebral proteins in the zone of edematous swelling around the tumor implanted into the brain.

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