ANAPHYLACTIC REACTIONS IN EXPERIMENTAL ALLERGIC ENCEPHALOMYELITIS

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Guinea pigs with experimental allergic encephalomyelitis develop an anaphylactic reaction after intravenous injection of brain tissue antigens. The intensity of the reaction reaches a maximum in the preparalytic period and diminishes with the appearance of neurological changes. The anaphylactic reaction with brain tissue antigens has a definite organ-specific character. The anaphylactic shock produced by intravenous injection of brain tissue antigens administered for sensitization in the early stages of the disease inhibits the subsequent development and course of the encephalomyelitis.

Allergenic stimulation in experimental encephalomyelitis, which is used as a model of demyelinating diseases in man, produced an integrated response of the immunologic system including various types of allergic reactions, some anaphylactic in character [1, 2].

The object of the present investigation was to study anaphylactic reactions at various stages of experimental allergic encephalomyelitis (EAE).

EXPERIMENTAL METHOD

Experiments were carried out on 100 female guinea pigs weighing 350-450 g. EAE was produced by a single intradermal injection of whole homogenized heterologous brain (monkey or rabbit) with Freund's adjuvant in the ratio of 2 :3.

Anaphylactic reactions were studied by the production of anaphylactic shock by intravenous injection of a reacting dose of antigen, consisting of a 20% saline extract of brain tissue with a protein content of 7-9 mg/ml as estimated by the micro-Kjeldahl method.

The intensity of the anaphylactic shock was assessed as follows: ± mild dyspnea, untidiness of the hair; + dyspnea, untidiness of the hair, scratching the mount with the paws; ++ sneezing, cough, scratching the mouth with the paws, slight disturbance of coordination; +++ convulsions, involuntary micturition and defecation, marked disturbance of coordination (not ending fatally); ++++ anaphylactic shock terminating in death.

EXPERIMENTAL RESULTS

In the course of EAE a state of increased sensitivity of the rapid anaphylactic type to brain tissue antigens developed by the 6th-8th day after injection of encephalitogenic material (Table 1). The intensity of the anaphylactic reactions reached a maximum by the 13th-18th day after reproduction of EAE, i.e., immediately before the appearance of neurological manifestations of the disease (experiments of series II). Reproduction of anaphylactic shock at this stage of the pathological process was followed by death of 18 of the 20 sensitized animals.

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TABLE 1. Intensity of Anaphylactic Shock at Various Stages of EAE

Series	No. of animals	Reproduction of EAE	Day after injection of encephalitogenic mixture	Neurological manifestations of EAE	Intensity of anaphylactic shock in sensitized guinea pigs					
					–	±	+	++	+++	++++
I	20	+	6-8th	–	6	4	1	4	5	–
II	20	+	13-18th	–	1	1	–	–	–	18
III	20	+	20-25th	+	–	–	–	6	14	–

TABLE 2. Effect of Anaphylactic Shock on Subsequent Development and Course of EAE

Series	No. of animals	Injection of encephalitogenic mixture	Reproduction of anaphylactic shock	Day of appearance of neurological changes					No. of animals developing disease	No. of animals dying
				15th	20th	25th	30th	35th		
I	10	+	+	–	–	–	4	2	6	3
II	10	+	–	6	2	–	–	–	8	7

In animals with neurological manifestations of encephalomyelitis the intensity of the anaphylactic reactions was appreciably reduced (experiments of series III). Although positive anaphylactic shock with brain tissue antigens was observed in all 20 affected animals, none of the animals died.

Animals developing anaphylactic shock became insensitive after a short time, and refractory to repeated injections of brain antigens. This state, described as desensitization, developed immediately after injection of the antigen and lasted for the next 2-3 weeks. The state of increased sensitivity was then restored, and the animals once again developed the typical picture of anaphylactic shock after intravenous injection of brain antigens.

If specific desensitization was produced on the 6th-8th day after reproduction of EAE by intravenous injection of 1 ml of 20% saline extract of brain tissue as used for sensitization, the neurological manifestations of the disease developed after a longer period (26-34 days) in 6 of the 10 animals; 3 animals died (Table 2).

In the control series of tests the latent period of the disease varied from 12 to 20 days; of 10 animals receiving the encephalitogenic suspension, 8 developed the disease and 7 died.

The character of the clinical picture as a whole (increased duration of the latent period, decrease in number of animals developing the disease and dying relative to the number of animals included in the experiment) and the uniform direction of the processes involved thus suggest that the reproduction of anaphylactic shock in early stages of EAE slightly retards its subsequent development.

When brain tissue antigens were injected on the 3rd-5th day after sensitization, a negative anaphylactic shock was observed in most animals, because a state of increased sensitivity of anaphylactic type no longer developed. These animals developed encephalomyelitis at the same times (2nd-3rd week) as the control animals without reproduction of anaphylactic shock. If, however, primary anaphylactic shock was produced in the animals at later periods (on the 10th-12th day after sensitization), as a rule these animals developed severe anaphylactic shock, often ending in death. Animals in which the anaphylactic shock at this time was negative or doubtful remained clinically healthy throughout the period of observation.

Reproduction of anaphylactic shock in animals with neurological changes had no significant effect on the subsequent course of the disease.

The anaphylactic reactions in EAE were of a marked organ-specific character. In guinea pigs sensitized with rabbit brain, for instance, moderate anaphylactic shock was observed with brain antigens from monkeys, guinea pigs, and man. However, the intensity of the anaphylactic reactions was less severe with antigens of homologous and heterologous brain tissue not used for sensitization. Intravenous injection of rabbit liver and testicular antigens into animals sensitized with rabbit brain tissue did not produce anaphylactic shock.

A state of increased sensitivity of anaphylactic type in animals sensitized with brain tissue can last for a long time. For instance, positive anaphylactic reactions of moderate intensity with antigens of brain tissue were observed in 9 of 10 guinea pigs one year after injection of the encephalitogenic material.

It is interesting to note that in some cases (6 of 10) a state of increased sensitivity of anaphylactic type was transmitted to the next generation born to animals in which EAE had been reproduced.

To summarize the results described above, EAE is accompanied by development of anaphylactic reactions whose intensity reaches a maximum in the preparalytic period and decreases in animals with the appearance of neurological manifestations of the disease.

The biological action of anaphylactic reactions differs at different stages of the pathological process during EAE. For instance, in the early stages of sensitization, reproduction of anaphylactic shock has a depressant effect on the subsequent development and course of encephalomyelitis. Reproduction of anaphylactic shock in animals in the preparalytic period causes death of the overwhelming majority of animals, whereas anaphylactic shock in animals with neurological changes had no significant effect on the subsequent course of the disease.

LITERATURE CITED

1. T. M. Tsaregorodtseva, in: Simpozionul National de Nauropatologie, 2d, Bucharest (1968), p. 171.
2. G. Voisin, in: Les Maladies avec Auto-Anticorps, Paris (1955), p. 225.