INFLUENCE OF ALLERGIC REACTIONS ON THE COURSE OF PREGNANCY IN ANIMALS

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Published data [1, 2] and also our own clinical-statistical observations show that among the causes of premature interruption of pregnancy toxicoses occupy one of the leading places.

Furthermore , a number of authors regard toxicoses in pregnancy as a manifestation of a general allergic reaction of the organism of the pregnant subject to placenta albumin.

Starting from this premise we decided to check experimentally the influence of sensitization by albumin on the course of pregnancy in animals (rabbits).

The necessity of arranging experiments is all the more justified since the question of the pathogenesis of premature birth has so far not been the subject of experimental investigation from the point of view of allergic factors.

EXPERIMENTAL METHODS

We conducted a series of experiments with five-time sensitization of animals with the albumin of horse serum and also with placenta albumin of heterogenic and homogenic origin, as usually employed as an allergen in experimental reproduction of allergic phenomena.

At the conclusion of sensitization the animals were paired and after pregnancy was established they were given a resolving injection with the same type of albumin in the conducting vessel of the cornu of the uterus, which was carried out by means of a laparotomy under general ether anesthesia.

A total of 5 series of experiments was performed.

In the first series (9 experiments) the animals were sensitized with introduction of 2 ml antidiphtheria serum on 5 occasions in the ear vein, and on the 19-23 day after coupling the resolving injection was administered after which, as a rule, all the animals 1-2 days later aborted premature and, in the majority of cases, dead rabbits.

EXPERIMENTAL RESULTS

Macro- and microscopic investigation of a number of organs (liver, kidneys, brain, womb) of the animals which died in the first days after abortion, showed the presence of the influences of an acute disturbance of blood circulation.

In the liver we observed everywhere stasis, hemorrhage along the Glisson capsule, perivascular hemorrhages between the hepatic fissures and also sections with foci of parenchymal necrosis.

In the kidneys hemorrhages were observed principally in the cortical layer. In the winding tubules there were foci of fine necrobiosis.

In the brain a picture of stasis was found; in individual sections there were contractions of the vessels and cellular proliferation around the vessels and in the vascular wall itself.

In the uterus there were fine hemorrhages, stasis and enlargement of the capillaries in the musculature. The mucous membrane was necrotized over a large area.

The same changes were found in the organs of the animals subjected to biopsy in the first few days after abortion.

In the experiments when biopsy was performed 1-2½ hours after abortion, the changes in the organs were marked by signs of proliferation.

In the liver we found single fine hemorrhages with a deposit of hemosiderin and organized thrombi, foci of peripheral cellular multiplication in individual lobules, a certain atypical character of the parenchyma and congestion of the central veins.

In the musculature of the uterus there were organizing thrombi and in places atrophy of the muscular wall; the mucous membrane of the uterus was in a state of atrophy.

In the 2nd series (9 experiments) we used an extract prepared from human placenta as antigen (10 g placenta tissue per 90 ml Locke-Ringer solution); the albumin content varied from 0.4 to 0.6% at pH 6.8-7.1. The method of the experiments was the same as in the first series.

In all cases 1-2 days after the resolving injection the animals bore premature, more often dead young.

The morphological changes in the animal organs were identical with the changes obtained in the first series of experiments, showing predominant localization in the vascular walls.

In order to prove the pathogenetic significance of the placenta albumin as an allergic factor responsible for the inception of premature birth, in the third series (10 experiments) the animals were sensitized with the placenta antigen of an animal of the same species.

For this purpose a 10% extract was taken from the placenta of the rabbits subjected to Cesarean operation. The method of conducting the experiments was the same as in the first and second series. In all the animals pregnancy was interrupted and they bore premature, mainly dead, young, 1-2 days after the resolving injection.

Macro- and microscipic study of the organs of the animals revealed the same changes as we saw in the first 2 series of experiments with degenerative changes of varying intensity.

Despite the law-governed reaction, manifest in interruption of pregnancy and the similarity of the morphological changes obtained in the first three series of investigations, two control series of experiments were undertaken to establish how preliminary sensitization without the resolving injection affects the course of pregnancy and whether the very fact of introducing the placenta extract in the conducting vessel of the cornu of the uterus does not exert an influence on the interruption of pregnancy.

In the fourth series (8 experiments) the nonsensitized pregnant animals were given 2 ml homologous albumin in the conducting vessel of the uterus cornu and in the fifth series 11 rabbits were first of all sensitized with homologous placenta albumin and after pregnancy was established 2 ml Locke-Ringer solution was administered to them in the artery of the cornu of the uterus.

The findings obtained in the experiments of the fourth series establish that introduction in healthy (nonsensitized) pregnant animals of 2 ml homologous placenta albumin does not lead to interruption of pregnancy which terminates with the birth of live on-time fetuses.

As for the microscopic investigation of the organs, the greatest changes in them were found in an experiment in which the rabbit died soon after parturition and when biopsy was performed 3-5 days after parturition. In those experiments where biopsy was performed on the 19 and 35 day after parturition the morphological changes were chiefly of a regenerative character.

In the fifth series (10 experiments) we sought to clarify the traumatizing influence of injection itself in the conducting vessel of the womb on the course of pregnancy in the rabbits, which had earlier been sensitized with placenta albumin. It was shown that introduction of Locke-Ringer solution in the vessel of the womb of the sensitized animals does not disturb the course of pregnancy and parturition in them occurs at term (average duration of pregnancy was 29-33 days).

Microscopic examination of the organs of four rabbits which died on the 5-8 day after parturition, showed the presence of a pronounced vascular reaction which was the same as in the earlier series of the experiments in the first days after the resolving injection with a different type of albumin.

In the experiments in which the animals survived and biopsy was conducted on the 20-35 day after parturition, the morphological changes were predominantly of a regenerative character.

In two experiments of this series the animals were killed 1 day after introduction of Locke-Ringer solution in the uterine artery in developing pregnancy. Upon autopsy of these animals we did not find any changes and upon microscopic examination of the organs a scarcely perceptible vascular reaction without the presence of hemorrhages and degenerative changes in the parenchymal organs was established.

The results of the fifth series of experiments showed that trauma inflicted on the cornu of the uterus in pregnancy with a resolving injection does not cause interruption of pregnancy.

Together with this it was established that parturition can in itself to a certain degree be a deciding factor and produce changes in the organism of the animals which are similar to the morphological picture in a typical allergic reaction.

In the sixth series of experiments we set out to clarify the course of pregnancy in sensitized animals with a resolving injection of placenta albumin in the outer vein of the ear and not in the conducting vessel of the uterus as in the preceding experiments.

For this purpose 10 rabbits were sensitized with introduction of homologous placenta albumin on five occasions, they were later coupled, and when pregnancy was established a resolving injection of allergen was introduced in the outer vein of the ear.

One to two days after the resolving injection all the rabbits gave birth, in the majority of cases, to dead young.

In 4 rabbits which died after abortion histological examination of the organs revealed the same changes as had been found in the animals in the first three series.

Consequently, these experiments established that the allergic reaction expressed in an interruption of pregnancy does not depend on the site of injection of allergen in the resolving injection.

The experimental investigations conducted showed that introduction in sensitized animals of a specific antigen both in the artery of the cornu of the uterus and intravenously in all cases leads to interruption of pregnancy.

The possibility of experimental reproduction of premature birth with sensitization and a resolving introduction of homologous antigen makes highly probable a certain degree of sensitization by the placenta antigen in the course of normal pregnancy.

However, the degree of sensitization achieved in the artificial conditions of an experiment may obviously arise in the course of natural pregnancy only at a certain level of reactivity of the organism determined by immuno-allergic relations and the functional state of the nervous system.

LITERATURE CITED

[1] A. I. Abrikosov, Sovremennoi Klinika 1933, Nos. 5-8.

[2] A. D. Ado, Arkh. Patol. 1951, No. 3, pp. 3-6.

[3] Ya. A. Dultsin, Collection Devoted to the 175th Anniversary of the Snegirev Home * (Leningrad, 1949).

* In Russian.

[4] B. A. Egorov, Klin. Med. Vol. 13, No. 12 (1935).

[5] B. A. Egorov, Klin. Med. Vol. 12, No. 9 (1935).

[6] A. D. Kaplan, Akusherstvo i Ginekol. 1939, No. 6.

[7] L. Z. Karelich, Med. Zhur. Byelo. 1940, 3-4.

[8] E. M. Kravets, Sovet. Vrachebny Zhur. 1938, No. 3.

[9] A. P. Nikolaev, Akusherstvo i Ginekol. 1947, No. 2.

[10] M. A. Petrov-Maslakov, Akusherstvo i Ginekol. 1952, No. 3, pp. 23-27.

[11] A. I. Serebrov, Akusherstvo i Ginekol. 1937, No. 1.

[12] G. M. Shkolyansky, Collection of Works of Members of the Leningrad Obstetrics and Gynecological Society during the War and Blockade* (1943), pp. 31-46.

*In Russian.