MAST CELLS AND VASCULAR PERMEABILITY IN RATS WITH EXPERIMENTAL ASEPTIC PERITONITIS

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UDC 616.381-002.021.4-092.9-07:[616.155.36+616.13/.14-008.6

KEY WORDS: mast cells; vascular permeability; aseptic inflammation.

In recent years the closest attention has been paid to mast cells which, as the present writers have shown, play an unambiguous role in the control of vascular permeability [4]. The histamine which is present in the mast cells of most species of animals and man is liberated from them under the influence of various pathogenic agents and gives rise to an acute increase in permeability of the venules, due to reversible structuralization and activation of the contractile system of the endothelial cells [2, 3].

The object of this investigation was to study the state of vascular permeability and the role of mast cells in its control in rats with experimental aseptic peritonitis induced by intraperitoneal injection of starch granules.

EXPERIMENTAL METHOD

Experiments were carried out on male albino rats weighing 180-220 g. Aseptic peritonitis was induced by intraperitoneal injection of 10 ml of a 3% sterile starch suspension in distilled water.

The state of permeability of the mesenteric microvessels was judged by the "labeled vessels" method [5] 1 h and 1-4 days after the beginning of development of peritonitis. The substance 48/80 (from Sigma, USA) was used as degranulator of the mast cells and was injected intraperitoneally as the 0.02% solution in a volume of 3 ml and intradermally in a volume of 0.25 ml. Exogenous histamine-OH (from Fluka, Switzerland) was injected intraperitoneally in a volume of 3 ml of the 0.01% solution. Three rats were used at each time of investigation during the different procedures.

The cell composition of the peritoneal fluid was studied in intact and experimental rats 1 h, 1-7 days, and 2 and 3 weeks after intraperitoneal injection of starch. To obtain peritoneal washings, 5 ml of Hanks' solution with heparin in a concentration of 5 units/ml was injected intraperitoneally into the guillotined rabbits. Laparotomy was performed 5 min later and the fluid aspirated and centrifuged for 5 min at 1000 rpm. The supernatant was poured off and the residue treated with 1 ml physiological saline, resuspended, and used to prepare films which were stained by the Romanovsky–Giemsa method. Six rats were used at each time of the investigation.

Mast cells in the mesentery were detected by staining with toluidine-blue [1] 2, 3, and 4 days after intraperitoneal injection of starch. Three rats were used at each time of the investigation.

EXPERIMENTAL RESULTS

A sharp increase in permeability of the mesenteric microvessels, chiefly venules, was found 1 h after intraperitoneal injection of starch (Fig. 1A). The vascular permeability also was increased, but to a much lesser degree, after 1 day (Fig. 1B). In the later stages of the investigation (2, 3, and 4 days after injection of starch) "labeled vessels" could no longer be detected, showing restoration of normal permeability of the venules.

To assess the possible effect of distilled water in which the starch suspension was made up on vascular permeability, the state of permeability of the mesenteric microvessels was studied 1 h and 1 day after intra-

Laboratory of General Pathology and Experimental Therapy, Institute of General Pathology and Pathological Physiology, Academy of Medical Sciences of the USSR Moscow. Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 91, No. 5, pp. 528-530, May, 1981. Original article submitted November 10, 1980.

0007-4888/81/9105-0575$07.50

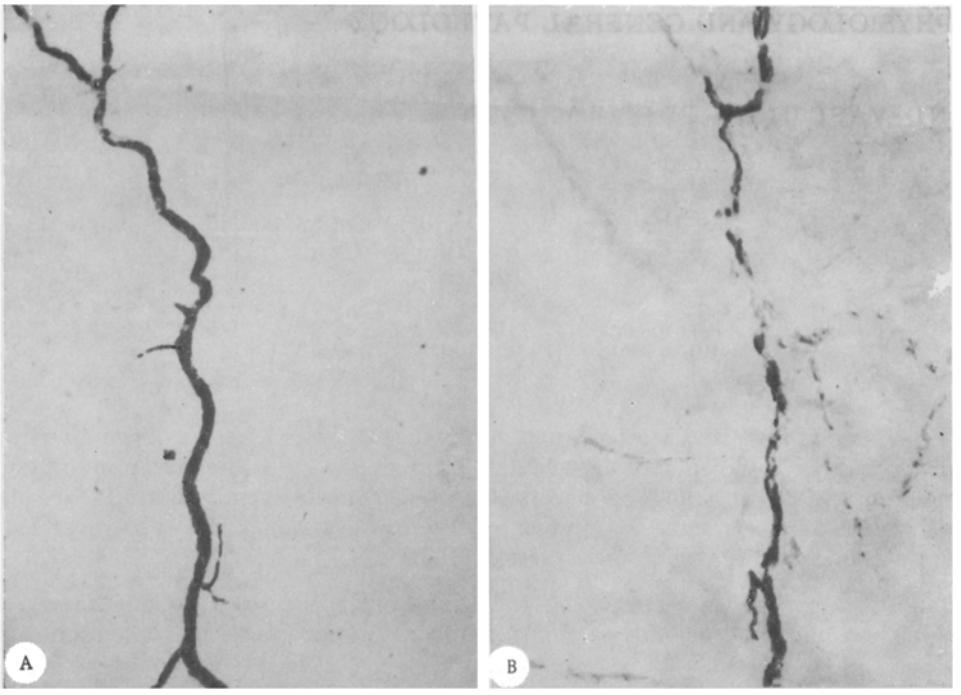

Fig. 1. Labeled vessels in mesentery of rat 1 h (A) and 1 day (B) after intraperitoneal injection of starch, 35×.

peritoneal injection of 10 ml sterile distilled water into rats. No labeled vessels could be found in the mesentery in any of the animals, proving that the disturbance of vascular permeability in this model of inflammation was due to the starch granules.

The study of the cellular composition of the peritoneal fluid showed that 1 h after injection of starch mast cells accounted for only 3 ± 0.4%, compared with 39 ± 3.8% in the intact animals. After one day no mast cells could be found in the peritoneal fluid. None were present likewise in the later stages of the investigation until the 21st day after the beginning of inflammation. These results suggest that starch granules induce pathological degranulation of mast cells, resulting in the liberation of histamine and serotonin, which disturb the permeability of the microvessels in a focus of inflammation, at times coinciding with a sharp decrease in the number of mast cells in the peritoneal fluid.

When these results are analyzed, special attention must be paid to the fact that one day after intraperitoneal injection of starch the mast cells had completely disappeared from the peritoneal fluid. No mast cells likewise were found histologically in preparations of the mesentery (2nd-4th day).

Disappearance of the mast cells in the focus of inflammation also was confirmed by the results of the other series of experiments. Intraperitoneal injection of compound 48/80 on the 2nd-4th day of development of peritonitis did not disturb the permeability of the mesenteric microvessels, as was observed in the control animals.

However, it can be claimed that at these times of development of inflammation the vessels are insensitive to histamine, which could perhaps be liberated in response to compound 48/80, but which did not act on permeability of the venules. To clear up this problem, on the 4th day of peritonitis histamine was injected intraperitoneally and a disturbance of permeability of the mesenteric microvessels was observed. This confirms that the ability of the endothelium of the microvessels to react to histamine was preserved. Consequently, the ineffectiveness of compound 48/80, described above, can be explained only by the absence of mast cells in the peritoneal cavity.

Further investigations showed that the mast cells disappeared and are not restored only in the focus of inflammation. This was shown by the results of experiments with intradermal injection of compound 48/80 on the 4th day of development of peritonitis. Permeability of the microvessels of the skin was substantially disturbed at the site of injection of compound 48/80, indicating that the mast cells were intact in the animals' skin and that they reacted normally to the action of the degranulator.

To determine the precise mechanism of action of starch on vascular permeability and, in particular, the ability of its granules to disturb permeability directly, i.e., without the participation of the mast cells, experiments were carried out in which 1 ml of a 3% sterile starch suspension was again injected intraperitoneally into rats on the 4th day of development of peritonitis when, as results of previous experiments showed, no mast cells were present in the focus of inflammation. The vascular permeability was undisturbed after repeated injection of starch.

These results suggest that the trigger mechanism of disturbance of vascular permeability in rats with "starch" peritonitis is degranulation of the mast cells and liberation of mediators of inflammation from them. This model of inflammation is particularly interesting because in this case a local focus can be formed, in which not only do all the mast cells disappear acutely, but their population is not restored for a long time, at least until after 3 weeks.

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ROLE OF SOME BRAIN FORMATIONS IN THE GENERATION AND SPREAD OF ALPHA-LIKE ACTIVITY IN DOGS IN THE EARLY POSTRESUSCITATION PERIOD

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UDC 616-036.882-08-036.8-07:616.831.314-073.97

KEY WORDS: electroencephalogram; generalized activity; spread over the brain.

Analysis of the electroencephalogram (EEG) of dogs in the early postresuscitation period revealed a regular appearance of definite forms of activity. In particular, in the presence of relatively severe hypoxia of the CNS, generalized rhythmic activity with the frequency of the α-rhythm and with maximal amplitude in the region of the amygdaloid nucleus (AN) and minimal in the cortex, appears on the EEG of dogs in the early stages of resuscitation [3]. It has been shown [3] that this activity appears earlier in AN than in other brain formations, and that a physical factor and the properties of the brain as a bulk conductor participate in its spread. These facts served as the basis for the suggestion that AN plays the leading role in the generation and spread of alpha-like activity over the brain. It is also known that when this activity reaches sufficient abundance on the EEG, delay is observed in recovery of other of activity [4, 5], possible evidence of the existence of physiological interaction with other formations in the generator of this activity.

The object of the present investigation was to clarify the role of AN and to discover the role of other formations of the cerebral hemispheres in the spread of generalized alpha-like activity over the brain.

EXPERIMENTAL METHOD

Experiments were carried out on 12 dogs weighing 10-14 kg. Before the experiment and after premedication with pantopon (8 mg/kg subcutaneously), glazed metal electrodes were inserted into AN, the ventral

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(Presented by Academician of the Academy of Medical Sciences of the USSR V. A. Negovskii.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 91, No. 5, pp. 530-532, May, 1981. Original article submitted July 8, 1980.