EFFECT OF BACTERIAL POLYSACCHARIDE FROM Pasteurella pestis ON DISTRIBUTION OF I^{131}-LABELED FIBRINOGEN IN MICE WITH CROCKER'S SARCOMA

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UDC 616.-006.3.04-092.9-092-02: 615.331]-073.916

Pyrogenic polysaccharide from Pasteurella pestis causes the selective accumulation of I^{131}-labeled fibrinogen in nodules of Crocker's sarcoma (sarcoma 180) transplanted into mice.

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Published data and the results of our previous investigations show that radioactive fibrinogen labeled with I^{131} is retained in human and animal tumors [1, 2, 8]. It is interesting to investigate the possibility of stimulating the retention of labeled fibrinogen in tumor tissue.

The object of the present investigation was to study the effect of pyrogenic polysaccharide from Pasteurella pestis on the distribution of human fibrinogen labeled with I^{131} in mice with a transplanted Crocker's sarcoma (sarcoma 180). Pyrogenic polysaccharides exert a selective influence on the blood vessels of tumors and can inhibit their growth [3-6, 7, 9, 10]. This applies also to the polysaccharide from P. pestis.

EXPERIMENTAL METHOD

Experiments were carried out on 133 noninbred male albino mice weighing 18-20 g. From 10 to 12 days after subcutaneous implantation of a Crocker's sarcoma the animals received an intravenous injection of 0.1 ml of a solution of human fibrinogen labeled with I^{131} (activity 0.5-0.6 μCi per mouse). Six hours later an intraperitoneal injection of pyrogenic polysaccharide was given in a dose of 0.05-0.1 mg per animal, made up in 0.1 and 0.2 ml, respectively, of pyrogen-free physiological saline, while control animals received an intraperitoneal injection of pyrogen-free physiological saline only in a volume of 0.1 and 0.2 ml per mouse. The animals were sacrificed by exsanguination 1, 3, 5, and 7 days after the injection of labeled fibrinogen. The methods of I^{131}-labeling of the fibrinogen and of determining radioactivity in each investigated organ and tissue were the same as those described in previous reports [1, 2].

Polysaccharides from P. pestis were prepared (L. A. Voznesenskaya) by extraction with phenol and water [11]. Preliminary tests showed that injection of this preparation into noninbred albino mice weighing 27-30 g in doses ranging from 0.01 to 0.2 mg per animal is not accompanied by visible toxic effects. Intravenous injection of the preparation into rabbits in a dose of 50 μg/kg caused an increase in temperature of 1.5-1.6°, lasting for 6 h. No extensive hemorrhagic foci of necrosis developed after injection of the preparation into mice with a transplanted Crocker's sarcoma, but a tendency was observed for growth of the tumor to be inhibited.

EXPERIMENTAL RESULTS

No macroscopically visible hemorrhages were found in the tumor nodules either in animals receiving labeled fibrinogen only or in those receiving fibrinogen and polysaccharide. This is particularly important because, as experiments have shown, labeled fibrinogen is retained in hemorrhagic foci in particularly large amounts, and in the presence of such foci, it would have been necessary to compare their

Laboratory of Combined Methods of Tumor Therapy, Institute of Experimental and Clinical Oncology, Academy of Medical Sciences of the USSR; Department of Medical Radiology, Central Postgraduate Medical Institute, Moscow (Presented by Academician N. A. Kraevskii, Academy of Medical Sciences of the USSR.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 68, No. 7, pp. 79-81, July, 1969. Original article submitted August 8, 1968.

activity with the activity of parts of the tumor without hemorrhages. In the animals receiving polysaccharide in a dose of 0.05 mg, activity of the tumor tissue at all periods of investigation was 1.6-3.5 times higher than in animals not receiving polysaccharide. In both experiments these differences were statistically significant after 1 and 3 days. At later periods statistically significant differences were found only in one experiment as a result of considerable variations in the specific radioactivity of the tumors.

To determine whether the increase in specific activity of the tumor tissue was linked with an increase in the intensity of selective retention of labeled fibrinogen in the tumors or whether it reflected a uniform increase in fibrinogen retention in various structures, the ratio between the specific activities of all investigated organs and of the blood and the specific activity of the tumors was calculated. In most cases these indices were lower in animals receiving polysaccharide than in those receiving physiological saline. However, this relationship did not always hold good. In experiment No. 23 it was completely upset after 5 days. Sporadic deviations were found in both experiments at other times also (experiment No. 23 – liver, spleen, and kidney after 1 day, skin after 3 days; experiment No. 30 – heart after 1 day, lungs, heart, liver, spleen, and skin after 3 days).

With an increase in the dose of polysaccharide to 0.1 mg per mouse, the results were much less systematic. This applies both to differences in the specific activity of the tumors and to differences in the ratio between the specific activity of the investigated normal tissues and that of the tumor. In this case no differences in the specific activity of the tumor could be detected after 3 and 7 days. In 11 of 28 determinations, no decrease was found in the ratio between the specific activity of normal tissues and the specific activity of the tumors.

These results show that retention of radioactive iodine bound with fibrinogen in the tissues can be intensified by means of pyrogenic polysaccharide. A selective increase in its retention in nodules of transplanted tumors can also be achieved. Further investigations are required in order to elucidate more fully the relationship between this effect and the dose of the preparation and also the conditions determining deviations of the results from the general rules. It would also be interesting at a subsequent stage to test other analogous preparations possessing marked pyrogenic activity in similar experiments.

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