Induced Resistance to a Transplantable Lymphatic Leukemia in Rats*

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(Received for publication June 14, 1941)

Early in the investigation of transplanted mammalian tumors, it was found that a resistant state could be induced by the injection of homologous living normal cells some days prior to the cancer inoculation.

Rhoads and Miller (5) have reported that immunity to transplantable leukemia in mice could be induced by the same method. MacDowell, Taylor, and Potter (2) extending this observation found that the induced protection depended on the genetic constitution of the immunizing tissue. Embryonic tissue from a highly inbred strain of mice did not induce resistance to inoculated leukemia in the same strain but the embryonic tissue from another strain or from hybrids of the inbred strains, was highly effective. In this laboratory Barrett (1) has demonstrated a similar relationship between the genetic make up of the normal tissue used for immunization and the degree of resistance induced to transplanted mouse tumors.

The present report is on an investigation of the induced resistance to a transplantable lymphatic leukemia of the rat (4). The strain was started from an animal in which the disease had been induced by an injection of dibenzanthracene. Like certain leukemias in mice, transplants of the cells may result in typical leukemia with lymphocytosis, and extensive involvement of the thymus and lymph nodes or the manifestation of the disease may be confined to a local lymphosarcoma. The original animal in which the condition was induced came from a subline of the Wistar Institute strain of rats and this strain has proved to be highly susceptible to transplants of the leukemia cells. About 90 per cent of those inoculated die of the disease in an average time of 9 days.

* This investigation was aided by a fund for leukemia studies contributed anonymously.

Experiments

Group 1.—This group is made up of four individual experiments and as the procedure was identical they are reported together. In each experiment a number of Wistar rats of the same age were divided into three lots. One of these was injected with cells from 18 day old embryos of the Wistar strain, one lot with defibrinated blood from adults of the same strain, and the third lot was kept for controls. The immunizing injections were given both subcutaneously and intraperitoneally. Some 12 days later all were inoculated intraperitoneally with 0.2 cc. of leukemic cells. The results are given in the first section of Table I.

Table I: Summary of Experiments

Immunizing material	Amount and location of injection	No. of rats Wistar strain	No. developed leukemia	Per cent resistant
Group 1				
Embryonic tissue from Wistar strain	0.2 cc. subcutaneously 0.3 cc. intraperitoneally	44	2	95.4
Defibrinated blood from adult Wistar rats	0.2 cc. subcutaneously 0.3 cc. intraperitoneally	21	3	85.8
Controls		41	37	9.5
Group 2				
Embryonic tissue from Wistar strain	0.5 cc. intraperitoneally	30	3	90.0
Embryonic tissue from Wistar strain	0.5 cc. subcutaneously	30	2	93.6
Controls		40	33	17.5
Group 3				
Embryonic tissue from hooded rats	0.5 cc. intraperitoneally	20	0	100.0
Embryonic tissue from hooded rats	0.5 cc. subcutaneously	20	5	75.0
Controls		20	18	10.0

Group 2.—There were three individual experiments in this group. The same procedure was followed as that used for group 1. One lot in each experiment was injected intraperitoneally with cells from 14 day old embryos of Wistar strain, one lot was given the same material subcutaneously. These, with the controls, were inoculated 12 days later. The results are given in the 2nd section of Table I.

Group 3.—The immunizing material for these animals was the tissue of embryos from the Rockefeller Institute strain of hooded rats. As with the preceding experiments, one lot was injected intraperitoneally and another subcutaneously with the immunizing normal cells and these animals with controls were inoculated with leukemia cells 12 days later. The results in two identical experiments are given in the 3rd section of Table I.

It is evident from the above experiments that a high degree of resistance is induced against transplanted leukemia in rats by a prior injection of homologous normal defibrinated blood or embryonic tissue. The embryonic cells from the Wistar strain were just as effective in the production of resistance as those from another strain, the hooded rats. The results were equally as good when the immunizing injections were given subcutaneously as when given intraperitoneally. As the leukemia inoculations were made intraperitoneally, this result would indicate that the resistance depended on a general reaction rather than a local one.

Summary and Discussion

It is known that a definite resistance to transplanted leukemia in mice may be induced by an injection of embryonic tissue prior to inoculation. The results of experiments reported in this paper establish the same fact for a transplanted lymphatic leukemia in rats. This emphasizes further the similarity between transplanted leukemia and malignant tumors. The important observation of MacDowell and his associates (2) that the immunizing power of the normal tissue depends on its genetic constitution, was not properly tested in the present study. However the principal is so well established that we are probably justified in assuming that the Wistar strain used was not genetically homogeneous because the embryonic tissue from the strain was just as effective in its immunizing property as the tissue from an unrelated strain. If this induced resistance is related to a sensitization phenomenon (3), as has been suggested, the tissues from a homogenous strain would cause no greater reaction than an autograft and no sensitization would result.

References

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