Heterologous Transplantation of Cancer of Childhood*

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The high degree of anaplasia and the early metastatic dissemination observed in many cancers of childhood suggest considerable autonomy of the neoplastic tissue, and readiness to transgress species barriers, as demonstrated by successful transfer into the anterior chamber of the guinea pig's eye.

During the past two years many of the malignant neoplasms submitted to the Department of Pathology of The Children's Hospital, Boston, were inoculated into the anterior chamber of the guinea pig's eye following the technic described by Greene (1). A total of 27 tumors were inoculated into 158 guinea pigs. The number of animals inoculated ranged from 1 to 20 (Table I). Most of these tumors were examples of the two most frequent retroperitoneal neoplasms in childhood, the embryoma of the kidney, and the neuroblastoma. Except in two cases the tissue was derived from surgical material, received sterilely, and within an hour after their removal.

Transplants were made subcutaneously, intraperitoneally, and intracerebrally, also, and into mice, rats, and rabbits. This report deals only with transplants into the anterior chamber of the guinea pig.

Successful heterologous transfers were not obtained with ease. In no instance was a "take" achieved with tissue from the embryomas or neuroblastomas. The only successful transfer was obtained with tissue from a congenital sarcoma, classified at that time as fibrosarcoma; in this case the growth began after a long incubation period (157 days), and in only one animal out of 18.

This neoplasm arose in the soft tissue of the calf of a newborn female infant (Fig. 1, 2 and 3) with a high cancer incidence in the maternal family. The tumor was poorly differentiated, (Fig. 4), metastasized early and widely, and led to death on the 98th day of life. The successful transfer was done on the 33rd day of life, following biopsy of the tumor; transfer of metastatic tissue, at autopsy, was not successful.

The tumor tissue, at the time of the successful inoculation, was soft, pale, and friable. The inoculation was done between 1 and 3 hours after surgical removal. It had been kept at room temperature, and suspended in sterile physiological saline solution most of this time.

A total of 18 animals were inoculated. In 12 of these the inoculum had been practically absorbed within 3 weeks, leaving only faint scars. One died of broncho-pneumonia after one week. No tumor tissue was found microscopically in the eye of this animal. One animal showed absorption after 8 weeks. In one animal an attempt at vascularization occurred after 5 weeks. Autopsy 2 weeks later showed granulation tissue only. A similar attempt was seen in another animal, after 12 weeks; this attempt was followed by absorption.

One animal, the twelfth of this series, was inoculated more than 2 hours after surgical removal. The inoculum remained stationary for 3 weeks, being located in the center of the anterior chamber, without apparent connection to the iris. During the following 5 weeks a faint gray, slowly growing halo was noted around the inoculum. Vascularization took place after 8 weeks, with the development of a small pink mass filling about one-fourth of the anterior chamber. This regressed, however, and at the end of 3 months only a pale gray scar remained. During the fourth month there was again some vascular growth, accompanied by what appeared to be a hemorrhage into the anterior chamber. Three weeks later another small pink mass was noted which grew steadily during the following 2 weeks to occupy a space measuring 0.6 × 0.6 cm. The animal was then sacrificed, 157 days after inoculation. Microscopic sections showed tissue

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more differentiated than the original tumor, and resembling a fibrosarcoma (Fig. 5).

Five animals were inoculated with the tissue obtained from the eye. In 3 of these the inoculum was absorbed within 2 weeks. One has remained stationary for 4 months. In another animal there was subtotal absorption during the first month. Vasculization and growth occurred during the first half of the second month, but again regression took place during the second half of this month. Ten weeks after inoculation vasculization again occurred, with increase in the size of the inoculum. The animal was sacrificed, 79 days after inoculation. The sections showed a fibrosarcoma, more cellular than after the first transfer, but still more differentiated than the original tumor (Fig. 6). Four more animals were inoculated with the growth obtained, but total absorption had occurred in all animals within 150 days.

DISCUSSION

It is reasonable to assume that the reported experiment represents a successful heterologous transplant of human neoplastic tissue. The morphological picture, the long incubation period, and the gross observations during this time make unlikely an inflammatory process of the iris of the host.

There is at present no explanation for the failure of the other inoculations.

SUMMARY

A successful heterologous transplant of a congenital human fibrosarcoma into the anterior chamber of a guinea pig's eye is reported. Heterologous transplants of 26 other human cancers of childhood, mostly embryomas and neuroblastomas, were unsuccessful.

NOTE: Since this paper was submitted, a successful heterologous transplant of an embryoma of the kidney was achieved in one out of 6 animals. There was a latent period of about 2 months. The microscopical structure was identical with that of an embryoma. Second generation transplantation into 2 animals was unsuccessful.

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REFERENCE


DESCRIPTION OF FIGURES 1 TO 3

Fig. 1.—Congenital fibrosarcoma of 33 days old infant, from which grafts were taken.

Fig. 2.—Roentgenogram of right calf showing involvement of soft tissue.

Fig. 3.—Roentgenogram of normal left calf of female infant.
Figs. 1-3
DESCRIPTION OF FIGURES 4 TO 6

FIG. 4.—Section of biopsy from congenital fibrosarcoma, (S-46-907).

FIG. 5.—First generation transplant in guinea pig’s eye after 157 days.

FIG. 6.—Second generation transplant after 79 days.
Figs. 4-6
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