A Histopathological Study of Heterologous Transplants of an Unusual Brain Tumor*

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The histopathological changes which are produced by the heterologous transplantation of human tumors have been studied for a number of years. Rather distinctive morphological alterations may occur (3) and may be useful, on occasion, in advancing the study of such transplanted neoplasms (Freeman and Zimmerman (2), and Willis (11)). On the other hand, Kniseley and Kernohan (7) feel that the method has distinct limitations in this regard. In a recent case, in which heterologous transplants of a human brain tumor were studied, certain morphologic features which occurred in the transplant and not in the primary tumor were observed. Since there had been considerable disagreement among competent neuropathologists as to precisely what the primary tumor was, and because the histopathological features of the transplants were very distinctive, a brief note on these findings seemed justifiable.

METHODS AND RESULTS

The original tumor material was obtained from the occipito-parietal region of a 7-year-old colored girl, whose preoperative clinical history extended over a period of 18 months. The tumor was located intracerebrally and was infiltrative. Microscopic sections of the tumor showed it to be made up of large, spherical tumor cells, approximately 25–35 μ, with abundant pink cytoplasm (Fig. 1). The nuclei were vesicular with a moderate amount of chromatin; some of them showed multinucleation or lobulation. An occasional cell had crescent-shaped nuclei at the margin of the cell. Atypical mitotic figures were frequent. Stroma formation was abundant; it contained an irregularly placed vascular bed.

The morphology of the original neoplasm suggested many possibilities for classification. Since Nissl, PTAH, Mallory, and Holzer stains and silver carbonate impregnations for microglia and astrocytes, as well as Hortega’s triple impregnations, did not reveal protoplasmic processes of the tumor cells, it was unlikely that the tumor was of neuro-ectodermal origin. The possibility of a mesodermal tumor, although suggested by a perivascular arrangement of the tumor cells, found little support from the results of special techniques. Azan stains revealed no collagen outside the venules and Wilder silver impregnations demonstrated no reticular fibrils other than in the perivascular areas. Inasmuch as the clinical history extended over 2 years, it was felt that a melanomatosis of the meninges should probably not be considered. This view was amplified further by the consistent lack of melanin in the tumor cells, by the notable rarity of melanomas among Negroes, especially in this age group, and by the demonstration of normal melanophores in the meninges infiltrated by the tumor.1 Several weeks after the biopsy, the child died. Autopsy revealed a brain tumor which evidently had originated from the site of operation and spread all over the right hemisphere, penetrating dura and skull, and invading the subgalea at the area of the craniotomy. Histologically, the tumor presented the same features as were revealed at the biopsy. Particularly impressive was the perivascular arrangement of the tumor cells where the neoplasm invaded the nerve tissues.

It was considered that transplantation could lead to further information pertaining to diagnosis. Therefore, tumor material, removed at surgery, was injected into a number of animals and 8-day-old embryonated chick eggs. When transplanted into the anterior chamber of the guinea pig eye, the tumor grew rapidly. Within 4 weeks, the anterior chamber was completely filled in four of six animals. Secondary transplants were also obtained in the same species. Primary and secondary transplants in the chick embryos sur-

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vived and grew moderately, but did not survive to the third generation. No takes were obtained after intracerebral or intraperitoneal injection in rats and mice, nor after injection into the anterior chamber of the rabbit's eye.

In the transplants in the anterior chamber of the guinea pig eye, the morphology of the tumor cells, while generally similar to the original, underwent certain changes. The tumor displayed an invasive tendency toward ecto- and mesodermal structures.

In the areas where the tumor had destroyed the iris (Fig. 2), the melanin of the pigment epithelium was dispersed, and a considerable number of tumor cells had engulfed and phagocytosed various amounts of melanin (Figs. 3 and 4). In some instances, the amount of foreign material in the cytoplasm was so great that the nucleus was pushed to the margin of the cell, where it assumed a crescent shape (Figs. 5 and 6). This was observed in three animals, but not in the fourth; this animal was an albino. Furthermore, the tumor cells became variable in size, the vesiculated nuclei were generally located in the center of the cell, and there was a definite decrease in the number of mitoses. However, no formation of cytoplasmic processes and no reticular fibrils were demonstrable by special stains.

DISCUSSION

The neoplasm studied developed invasive and destructive properties in heterologous transplants, which Greene and co-workers (5, 8) and Martin (9) consider to be a definite sign of malignancy. In addition, the dispersion of melanin in the transplants suggested the tumor was some type of sarcoma, as shown by Freeman and Zimmerman (2).

Further identification along these lines was not feasible, since the cytomorphology did not correspond with any known type of primary intracranial sarcoma. At that stage of the study, it was felt that the biologic behavior of the tumor cells might be utilized for diagnostic purposes rather than the tumor morphology. In other words, was the phagocytosis seen in the transplants indicative of a tumor of reticuloendothelial origin?

Phagocytosis of particulate matter by tumor cells does not occur, according to Willis (11). Ackerman (1) maintains that this feature is indicative of reticulum-cell sarcomas. Although tumor cells are frequently invaded by leukocytes or even seen to ingest necrotic elements, as frequently seen in smear and touch preparations, true phagocytosis of melanin has not been reported in the literature, as far as we can see. Freeman and Zimmerman reported dispersion of the iris melanin in cases of transplanted sarcomas. It is difficult to determine from their article whether actual phagocytosis occurred.

It is thought that growing transplants still reflect, to some extent, the properties of the original tissue. The tumor studied was considered to have originated from reticuloendothelial elements, since they are known to possess phagocytic abilities. While special stains failed to reveal heavy fibrils, such have not been shown to be prerequisites for such tumors (Roulet [10]). Although cytomorphologically this is quite a diverse group, our tumor seems to be closely related to other observations of so-called primary reticulum sarcoma of the brain (6). Kinney and Adams (6) observed phagocytosis in the original neoplasm which they reported, which is further support of this interpretation. 3

A conclusion which finally might be drawn suggests that primary intracranial sarcomas originating from reticuloendothelial elements are not necessarily composed of uniform round cells about 15 μ in diameter, as proposed by Hanbery and Dugger (5), but may occasionally display pleomorphism and cells of varying sizes.

SUMMARY

When transplanted into the anterior chamber of the guinea pig eye, an unusual brain tumor displayed invasion and destructiveness to the structure of the eye. It also led to a dispersion of the melanin of the iris. Large amounts of melanin were phagocytosed by the transplanted tumor cells.

In an attempt to classify this tumor, a neuroectodermal growth or a melanomatosis of the meninges could be ruled out. Morphologic alterations of the tumor in the transplants were interpreted as being consistent with a tumor originating from reticuloendothelial elements.

3 Dr. Kinney, who was present at the time of the presentation before the American Society for Experimental Pathology, concurred with the diagnosis of reticulum-cell sarcoma.

REFERENCES


Fig. 1.—Tumor biopsy from right temporo-parietal area. Cells are rather anaplastic. They have abundant pink-staining cytoplasm. The nuclei are vesiculated and frequently crescent-shaped. Hematoxylin-eosin stain. Mag. ×850.

Fig. 2.—Tumor transplant in the anterior chamber of the guinea pig eye. The tumor invades the iris; nuclei of the tumor cells are usually located in the center of the cell. Toluidine blue stain. Mag. ×212.

Fig. 3.—Transplant. Several tumor cells contain various amounts of melanin (arrows). Hematoxylin-eosin stain. Mag. ×400.

Fig. 4.—Transplant. Tumor cells engulf lump of melanin. There are some double-nucleated cells. Hematoxylin-eosin stain. Mag. ×400.

Fig. 5.—Transplant. Many tumor cells are filled to capacity with melanin. The nucleus is pushed to the cell margin. Hematoxylin-eosin stain. Mag. ×400.

Fig. 6.—Transplant shows one tumor cell which contains large amounts of melanin. Many other cells show minute inclusions of melanin. Hematoxylin-eosin stain. Mag. ×400.
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