Recently we became interested in studying the cellular components of bronchial secretions in cases of pulmonary neoplasms. For this study it became necessary to have an experimentally produced lung cancer in small laboratory animals. We required a tumor which grew in uniform fashion and which behaved biologically in similar manner in different animals of the same species. Furth (1) reported on the inoculability of mice lungs to transplanted tumor cells. The following report is a description of the technique of transplanting into and producing tumor growth in the lung of the rabbit.

MATERIAL AND METHODS

For this study we used Brown-Pearce carcinoma of the rabbit. This tumor was originally discovered and described by Brown and Pearce (2) in 1923. The tumor is a highly malignant epithelial neoplasm which was first successfully transplanted by Brown and Pearce into the testes. The tumor spreads by way of the lymphatics producing widespread visceral metastases. Histologically the tumor is an undifferentiated, anaplastic carcinoma.

Thirty-five rabbits were used for this study. Rabbits were chosen at random from stock supplies without regard to sex, color or weight. In general, large, adult, healthy rabbits free of respiratory infections, as far as could be ascertained, were chosen. Large rabbits were selected to facilitate laryngoscopy, the technique of which will be described below.

Tumor tissue used for the transplantation was prepared as follows: portions of healthy, actively growing tumor were removed from stock tumor rabbits, using aseptic surgical technique. Necrotic portions of tumor were discarded. The tumor tissue was minced with a curved scissors and further crushed in a tissue press. A small amount of isotonic saline was added to the crushed tumor tissue in sufficient quantity to produce a thick suspension. This thick suspension was used for transplantation.

For transplantation the rabbits were anesthetized by intravenous administration of nembutal. A solution containing 25 mg. of nembutal per cc. was administered intravenously until the animals were lightly anesthetized. About 1 cc. of this solution per kilogram of body weight was usually required. With the animals anesthetized a small, child’s type, laryngoscope was introduced enabling direct visualization of the vocal cords. A size 8 French rubber catheter was introduced through the laryngoscope into the trachea and gently inserted to the bifurcation. Two cc. of the suspension of tumor tissue which had been previously prepared was then injected with gentle pressure from a Luer syringe through the catheter into the lumen of the trachea. The laryngoscope and catheter were then removed and the animal held in a vertical position to permit drainage by gravity of the injected tumor tissue into the lungs.

RESULTS

Successful tumor growth was obtained in 29 or 83 per cent of the 35 rabbits transplanted with tumor by this technique. It should be noted that the six rabbits in which there was no growth of tumor all comprised a group which were transplanted from the same batch of tumor tissue. The reason for the unsuccessful transplants cannot be determined, but it is quite likely that the tissue did not contain viable tumor cells.

Animals were sacrificed at varying intervals beginning at the 6th day after transplantation. At the 6th day tumor could not be identified grossly in the lungs. However, at this stage tumor could be readily identified microscopically (Figs. 1 and 2). On the 10th to 12th day following transplantation small nodules of tumor tissue could be identified grossly in the lungs and occasionally in the mucosa.
FIG. 1.—Brown-Pearce carcinoma nodule in lung, 6 days after transplantation when tumor was not visible grossly. (Hematoxylin and eosin preparation, X100.)

FIG. 2.—Similar field as Fig. 1. (Hematoxylin and eosin preparation, X400.)

FIG. 3.—Upper respiratory passages and lungs of rabbit that died 4 weeks after intratracheal transplantation with Brown-Pearce carcinoma. Note multiple tumor nodules throughout both lungs.

Fig. 4.—Larynx and trachea of rabbit that died 32 days after intratracheal transplantation with Brown-Pearce carcinoma. Note tumor nodules in wall of trachea.
of the trachea and bronchi. Since in the early stages tumor was found only in the lungs, it seems likely that the tumor growth within the bronchi and trachea was secondary to the “primary” tumor within the lung. Death usually occurred between the 51st and 38th day after transplantation. In animals which were permitted to die of tumor growth, both lungs were studded with myriads of tumor nodules measuring up to 1 cm. in diameter (Figs. 3 and 4). Death in these animals was usually due to asphyxia from occlusion of the stem bronchi by tumor masses and frequently superimposed pneumonia. Metastases to the liver were observed in a few cases. It should be pointed out that the absence of higher incidence of metastases was probably due to the fact that the animals died of the massive involvement of the lungs by the tumor growth before the neoplasm had had adequate opportunity to become disseminated.

Histologically the tumor nodules in the lungs were similar in their morphology to that originally described in testes and other organs. Necrosis of the tumor occurred early. The tumor was very cellular consisting of masses of epithelial cells with very little stroma. The cells varied markedly in size and shape as well as intensity of staining reaction and numerous atypical mitotic figures were seen. The cells varied from round or oval to polygonal. They had abundant, coarsely granular cytoplasm and pale, round or oval, vesicular nuclei containing one or more prominent nucleoli. In the advanced tumor areas of necrosis were common.

SUMMARY

A technique of transplanting tumors into the lungs of rabbits is described. Successful transplantations were accomplished in 29 of 35 rabbits used in this study.

REFERENCES

Intratracheal Transplantation with the Brown-Pearce Carcinoma


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