The Induction of Mammary Cancer in Male Mice by Isologous Pituitary Implants*

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SUMMARY

Hybrid (C3H/A) male mice which had received isologous pituitary implants developed mammary tumors. Since the incidence of spontaneous tumors in these mice is extremely low, the fact that thirteen out of 47 (27 per cent) mice given implants developed mammary tumors is highly significant. The histology was comparable to that found in corresponding tumors in the female.

Spontaneous mammary cancer in male mice is extremely rare, being noted only in the H strain of mice (1). We ourselves have discovered only one case, a fibrosarcoma in a 32-month-old C3H/A hybrid with an interstitial-cell tumor of the testis, presumably due to the endocrine imbalance of old age. Mammary carcinomas have, however, been induced in male mice by estrogens (2) or by ovarian grafts (7), and these are thought to act by stimulating an output of prolactin from the pituitary (6). We thought, therefore, that it might be profitable to implant pituitaries into intact male mice to ascertain the effect on the mammary gland, since implanted pituitaries are a source of prolactin. It had already been noted that there was an increase in iron in the mammary gland in both males and females after pituitary implantation (8), but we wished to observe this further.

MATERIALS AND METHODS

A pilot experiment was set up. The animals were all hybrid male mice bred from C3H male and A/Jax female mice. Both parental strains were known to carry the mammary tumor virus, and the incidence of spontaneous mammary tumors in the F1 female hybrid was 11 per cent at 10 months of age (8). All animals were fed Purina Fox Chow and tap water ad libitum. There was no evidence that either of these was contaminated with estrogens.

The first experimental group consisted of 26 male mice, each of which was given implants at 3 months of age of three male pituitary glands from similar F1 hybrid mice. The implants were inserted subcutaneously over the hip. A second group of 21 mice was similarly given implants of three female pituitaries. Both groups were kept either until they died or until a tumor developed, in which case they were sacrificed and tissues taken for histological study.

RESULTS

In the first group given implants of male pituitaries, eight of the mice developed tumors in the mammary region. These tumors developed between 9 and 26 months of age, with an average tumor age of 16 months.

In the second group given implants of female pituitaries, five tumors were found, developing between 12 and 25 months of age, with an average of 19 months. Thus, out of 47 male mice, thirteen developed mammary tumors.

Pathology.—The mammary tumors varied from 0.5 to 4 cm. in diameter and were firm. On incision a few of the larger ones had necrotic centers, but they were mostly solid.

Microscopically, all except one of the mammary tumors were adenocarcinomas of type B (National Cancer Institute classification [3]). The picture varied considerably from one tumor to another, but they all showed acinar formation with epithelial proliferation in some areas. Some had variable amounts of stroma. The one tumor which was not an adenocarcinoma was thought to be a fibrosarcoma, composed of bundles of spindle cells. Other mammary glands showed only isolated areas of development, but these were heavily loaded with iron, as in previously reported instances (8).

Examination of the implanted pituitary glands characteristically showed a well vascularized graft, the same size or a little smaller than a normal pituitary gland. Microscopically there was a typical fibrous capsule, a large number of chromophobes, a few eosinophils, but no basophils.

DISCUSSION

In the females of this hybrid stock mammary tumors frequently arise spontaneously and also are readily induced by isologous pituitary implantation (8). In males, however, since no spontaneous cases of mammary cancer have been reported except for our previously mentioned case in an old mouse, any tumors appearing in males under experimental conditions are significant. Out of these 47 male mice with implants, thirteen developed mammary tumors,

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TABLE 1

INCIDENCE OF MAMMARY TUMORS IN HYBRID MALE MICE AFTER
PITUITARY IMPLANTATION

<table>
<thead>
<tr>
<th>Implanted pituitaries</th>
<th>No. of mice</th>
<th>No. tumors</th>
<th>Percentage incidence of tumors</th>
<th>Av. tumor age (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 male</td>
<td>26</td>
<td>8</td>
<td>31</td>
<td>16 (range, 9-26)</td>
</tr>
<tr>
<td>3 female</td>
<td>21</td>
<td>5</td>
<td>24</td>
<td>19 (range, 12-25)</td>
</tr>
<tr>
<td>Total:</td>
<td>47</td>
<td>13</td>
<td>28</td>
<td>17</td>
</tr>
</tbody>
</table>

and the histology of these tumors was comparable to that of tumors found in females of the same stock. Our results were, therefore, considered to be of significance.

It has already been shown that, on implantation of isologous pituitary glands, the implanted gland is released from the inhibition of the hypothalamus and produces prolactin in greater quantity than normal (4, 5). The prolactin is thought to act directly on the mammary gland of females either as a carcinogen (6) or by preparing the mammary gland for the action of other carcinogenic agents (8). There is as yet no evidence of an exogenous source of estrogens for these mice, although the possibility cannot be ruled out that some natural ingredient of the food, such as alfalfa, could at this time have contained a minimal quantity of estrogen.

This report indicates that the same mechanism applies in male mice as in female mice of this hybrid stock.

Further work is now being done to test the effect of similar implantations in other strains and to study the effect of castration in these animals.

REFERENCES

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