SPONTANEOUS MAMMARY CARCINOMA IN A FEMALE RABBIT

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Spontaneous tumors in the rabbit are rare, particularly breast tumors. Few reports of mammary growths in this species appear in the literature, and all writers are agreed as to their infrequency.

Polson (1) reviewed the records published prior to 1927, citing 52 cases of tumors in the rabbit. To these he added 14, bringing the total to 66. Statistics available at the time of his report showed that among 1100 rabbits, 13 had spontaneous tumors, the uterus being the most frequent site. One case of mammary carcinoma in a rabbit is reported by Marie and Aubertin (2), as seen by P. Masson. Another case is referred to as mentioned by Bashford (3). This is probably the tumor to which Polson refers in his paper (Case 8), for which a slide was sent him by J. A. Murray. Since Polson's report in 1927, the most comprehensive review is that of Gaston Fardeau in 1931 (4). Fardeau adds no new examples of breast carcinoma and introduces his chapter on mammary rabbit tumor with a brief statement that "up to the present" these have been rare.

Ratcliffe (5), in a review of all tumors in wild birds and mammals dying in the Philadelphia Zoological Gardens from 1901 to 1932, mentioned no mammary tumor in the wild rabbit. Cutler (6), also, appears to have found no cases of breast tumors in his review of new growths in the rabbit.

Koyama (7) recorded the presence of lactation in a rabbit with multiple adenomata of the uterus, and Watrin and Florentin (8) report the occurrence of lactation and enlarged mammary glands in a rabbit that had littered three years previously, and which showed in the enlarged, congested uterus, a deciduoma. Fifer (9) described various changes in the mammary glands of 90 rabbits, but makes no mention of the presence of breast tumors in any of them.

The tumor here reported was observed March 30, 1936, in a white female rabbit about six years old, among the stock rabbits in the Crocker Laboratory. It was located in the region of the right upper mammary gland and extended upward to the clavicle and downward well beyond the subcostal margin, invading the right axilla laterally and covering the chest beyond the median line to the left. The growth was hard, nodular, and freely movable, measuring 20 × 8 × 3 cm. and weighing 340 gm. (Fig. 1). Numerous clear cysts, varying in size from 1 to 10 cm. in diameter, were present in the irregular mass (Fig. 2). In places the overlying skin was atrophic and adherent, but the growth itself did not infiltrate either the skin or underlying muscle. It was encapsulated and showed scattered areas of focal necrosis. On removal of the skin the tumor was found to be of a pearl-gray color, and dotted with hemorrhagic or discolored areas.
Histologic Pathology: The growth was encased in a thick fibrous capsule with septa surrounding lobes and lobules. The structure as seen under low magnification is diverse. The glands vary in architecture from simple tubular and simple saccular to branching forms, and show all grades of transformation to a papillary cystadenomatous structure with final development into carcinoma (Fig. 3). Some areas resemble the picture seen in Schimmelbusch’s disease of the human female. Other areas show masses of large epithelial cells filling lobules, as in the medullary type of carcinoma (Figs. 4 and 5).

FIGS. 1 AND 2. GROSS APPEARANCE OF SPONTANEOUS RABBIT TUMOR AFTER REMOVAL.
Fig. 1 (above) shows the lobulated character of the growth. Fig. 2 shows carcinomatous and cystic areas revealed on section.

In many of the cysts papillary projections are present, growing into the lumen. In addition to the epithelial proliferation in the cysts a considerable degree of necrosis, organization, and inflammatory reaction is apparent (Fig. 3). The epithelium in some of the papillae shows evidence of functioning as it exhibits fat globules of the type present in the breast of the pregnant or lactating female (Fig. 6).
In the carcinoma, giant cells and mitoses are frequently found (Figs. 7 and 8). At the periphery of the tumor are many venous emboli (Fig. 10).

The histology of the tumor as a whole is extremely varied. The carcinomatous areas are surrounded by papillomatous and adenomatous structures. The cells are equally variable (Fig. 3). In some areas it is impossible to say whether the structure is carcinoma or simple hyperplasia.

With the exception of extensions into neighboring vessels (Fig. 9), no metastases were found in the nodes or in the viscera. In sections of the left lower mammary gland there is evidence of chronic cystic mastitis. The ovaries show extensive luteinization and cyst formation. A few maturing follicles are seen. The uterine glands are involuted. Sections of the adrenals, pituitary, and thyroid glands failed to reveal any abnormal structures. No gross metastases were found in any of the organs.

On May 30, 1936, the tumor was removed under aseptic conditions, and twelve fragments, about 0.03 gm. each, were implanted subcutaneously under the mammary glands of four white female rabbits, one, two, three, and five years old. After two months three of the rabbits showed a few growing nodules at the site of inoculation, although most of the grafts appear to have been absorbed.
FIGS. 4 AND 5. SPONTANEOUS MAMMARY TUMOR IN THE RABBIT: MEDULLARY CARCINOMA FILLING OUT ENTIRE LOBULES. X 125 AND 220

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Fig. 6. Spontaneous Mammary Tumor in the Rabbit: Papillary Cystadenoma, Showing Functioning Epithelium. × 280

Fig. 7. Spontaneous Mammary Tumor in the Rabbit: Showing Giant Cells. × 280
FIG. 8. SPONTANEOUS MAMMARY TUMOR IN THE RABBIT: SECTION UNDER HIGH MAGNIFICATION TO SHOW VARIOUS STAGES OF ACTIVE MITOSIS. × 900

FIG. 9. SPONTANEOUS MAMMARY TUMOR IN THE RABBIT: EXTENSION OF NEOPLASM INTO ADJACENT VESSELS IN THE PERIPHERY OF THE TUMOR. × 120
FIG. 10. FIBRO-ADENOMA IN RABBIT'S BREAST PRODUCED BY ANTUITRIN S AND THEELIN. × 140

FIG. 11. FIBRO-ADENOMA IN RABBIT'S BREAST PRODUCED BY ANTUITRIN S AND THEELIN, SHOWING GLAND FORMATION AROUND TERMINAL DUCT. × 270
FIG. 12. CYSTADENOMA OF RABBIT'S BREAST PRODUCED BY ANTUITRIN S AND THEelin,
SHOWING LOBULE FORMATION AROUND DILATED DUCT. × 135

FIG. 13. CYSTADENOMA IN RABBIT'S BREAST PRODUCED BY ANTUITRIN S AND THEelin,
SHOWING MANY CYSTS. × 270
It is interesting to note that the histologic picture following the subcutaneous injection of antuitrin-S and theelin\(^1\) in old female rabbits in some ways closely mimics that of the benign areas of the neoplasm just described. Beginning in March 1933, the mammary glands of old female rabbits were injected with varying dosages of antuitrin S, 100–200 rat units, and theelin, 50–100 rat units, for periods of two months to two years. The changes produced in the breasts ranged from simple hyperplasia to intermediate stages of lactation, chronic cystic mastitis, and finally papillary cystadenomata (Figs. 10–13). The resemblance of these artificial growths to the tumor described above is quite striking. Outside the limits of the carcinomatous areas, it is difficult to differentiate between the spontaneous growth in the one rabbit and the induced growths occurring in seven others. It has, however, been impossible to produce malignant changes in the induced growths in spite of prolonged injections.

**Conclusion**

A spontaneous carcinoma in the right mammary region of a white female rabbit is described. The morphology of the tumor was complex, varying from simple and lactation hyperplasia to benign fibro-adenoma, papillary cystadenoma, and adenocarcinoma. No metastases were found in lymph nodes or viscera. Histologically the spontaneous tumor resembled in many respects that induced in seven rabbits by the injection of hormones.

**References**


\(^1\) For these hormones the author is indebted to Parke Davis & Co.