A Spontaneously Occurring Renal Tubule Carcinoma in a Mouse

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Abstract: Spontaneous occurrence of renal tubule carcinoma in mice is known to be rare. The following features of this tumor are recognized as areas of hemorrhage and massive necrosis and many show atypical cells and numerous mitotic figures. The present renal tubule carcinoma developed in an untreated B6C3F1 male mouse at the age of 109 weeks. The tumor mass occupied nearly the entire renal cortex and invasion of normal renal tissue was observed. The tumor had solid cell nests, a gland-like structure, definite neovascularization and capsular invasion. The tumor cells had clear eosinophilic cytoplasm, a brush border structure and high proliferative activity. Although tumors derived from the proximal tubule reportedly show basophilic cytoplasm, the tumor cells in this mouse had clear eosinophilic cytoplasm. Consequently, the animal was diagnosed as having an unusual renal tubule carcinoma (classification: solid type).

Key words: renal tubule carcinoma, kidney, B6C3F1 mouse, spontaneously occurring tumor

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Table 1. Spontaneous Renal Tubule Carcinoma in B6C3F1 Mice in the Literature and the Present Case

<table>
<thead>
<tr>
<th>Histological diagnoses</th>
<th>Male</th>
<th>Female</th>
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<tbody>
<tr>
<td>Adenocarcinoma [6]</td>
<td>1 / 2,543 (0.03%)</td>
<td>2 / 2,522 (0.07%)</td>
</tr>
<tr>
<td>Adenocarcinoma [5]</td>
<td>2 / 1,130 (0.18%)</td>
<td>0 / 1,130 (0.00%)</td>
</tr>
<tr>
<td>Renal tubule carcinoma*</td>
<td>3 / 1,650 (0.18%)</td>
<td>0 / 1,750 (0.00%)</td>
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</table>

[ ]: reference number. *: Our cases, including present animal.
Fig. 1. Transverse section of the left kidney showing a nodular tumor involving mainly the cortex.

Fig. 2. (a) Capsular border invasion of tumor cells into normal renal tissue (*). H&E, ×20. Bar = 0.5 mm. (b) Small areas of necrosis in the tumor (arrows). H&E, ×330. Bar = 20 µm. (c) In the cell nest, tumor cells show dense proliferation and a gland-like structure. Silver impregnation, ×150. Bar = 10 µm. (d) High magnification of (a). H&E, ×400. Bar = 20 µm.
of the tumor cells. The standard labeled streptavidin biotin technique was performed using a DAKO LSAB Kit. Formalin-fixed kidney tissues from a control 109-week-old male mouse were also prepared for comparison. For electron microscopy, small pieces of formalin-fixed material were prefixed with 2.5% glutaraldehyde and 2% paraformaldehyde in 0.1 M phosphate buffer and post-fixed with 1% OsO4 0.1 M phosphate buffer. After dehydration through a graded ethanol series, the samples were embedded in Epon 812 resin (Nakarai Tesque Inc., Kyoto, Japan). Ultrathin sections were prepared and stained with 4% uranyl acetate and lead citrate, and examined with a transmission electron microscope (H-7000, Hitachi High-Fielding Corp., Tokyo, Japan).

At necropsy, a white solitary nodule (28 × 18 × 16 mm) occupying most of the renal cortex was found in the left kidney. Other findings included an atrophic spleen and thymus, white spots in the stomach, nodules of the preputial glands and hypertrophic Harderian glands. Tissue trimming of the renal tumor revealed a clearly demarcated white nodule occupying nearly the entire renal cortex (Fig. 1).

Histological findings included a capsular border between the tumor and normal renal tissue, but tumor cells had partially invaded the fibrous capsular and surrounding tissues (Fig. 2a, H&E). Only a small area of necrosis was noted within the tumors (Fig. 2b, H&E). Edema and neovascularization were prominent in the tumoral stroma. The tumor was characterized by numerous solid cell nests showing closely compacted proliferative cells with a thin interstitium. Some of the cell nests showed closely compacted proliferative cells with a gland-like structure (Fig. 2c, silver impregnation). Tumor cells were stained clearly eosinophilic and showed cubic cytoplasm with a round or ovoid nucleus and minimal cellular atypism (Fig. 2d, H&E). There were two types of areas, one of which consisted of uniform sized cells and the other of various sized cells. Mitotic figures were occasionally observed. The PAS reaction revealed a few PAS-positive areas on the luminal side of the glandular lumen. Immunostaining of PCNA demonstrated an increased PCNA labeling index (22%) as compared with normal tissue (2%). These findings suggested that cell proliferative activity was enhanced in the tumor cells. Ultrastructural observation also confirmed the basement membrane, desmosomes, cell surface brush border structures, invaginations of the cell membrane, mitochondria, rough endoplasmic reticulum, glycogen granules and the concentric structure of lysosomes (Fig. 3).

The morphological characteristics of the tumor described above indicated the tumor was possibly derived from the renal epithelium. The brush border structure of the cell surface, Desmosomes (arrows), granular endoplasmic reticulum and glycogen in the cytoplasm can be seen. Bar = 100 nm.

Fig. 3. Electron micrograph. Brush border structure of the cell surface. Desmosomes (arrows), granular endoplasmic reticulum and glycogen in the cytoplasm can be seen. Bar = 100 nm.

neovascularization and highly proliferative activity. The features of this tumor suggested, in general, a malignancy. Therefore, the tumor was diagnosed as a renal tubule carcinoma (histological classification: solid type).

Spontaneous renal tubule carcinoma is a rare tumor in both rats and mice. Certain diagnostic features of this malignancy are recognized: areas of hemorrhage, necrosis, marked compression of surrounding normal tissue, infiltration of tumor cells into the adjacent parenchyma and prominent neovascular ingrowth. Cell morphology shows a wide range of atypism, from differentiated to pleomorphic and even occasionally anaplastic cell types. Mitotic figures may well be numerous, but are infrequent in some cases1–3,7–13. As for the histological features of this mouse, prominent neovascular ingrowth was recognized, but there was no hemorrhage, only slight cellular atypism, and necrotic foci were small and submicroscopic. Therefore, the morphological characteristics of the tumor differed somewhat from the usual histological features of renal tubule carcinoma. Renal tubule tumors originating from the proximal tubules of both mice and rats have also been known to show basophilic cell staining1,14. However, in the present mouse, the tumor cell cytoplasm showed a clear eosinophilic

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staining pattern, just like oncocytomas which are known to be derived from collecting tubules. Oncocytomas are characterized by homogeneous or fine granular cells with abundant eosinophilic cytoplasm. The tumor cells of an oncocytoma have round or oval nuclei with loose chromatin and indistinct cell borders. Ultrastructurally, the cytoplasm contains densely packed atypical mitochondria\textsuperscript{1,11,14}. Therefore, the histological characteristics of the present tumor were different from those of an oncocytoma.

The lack of massive tumor necrosis in this animal was considered to be due to prominent neovascular ingrowth in the central portion. The histological features described above differ from those of ordinary renal tubule carcinomas and are apparently unique, making this atypical tumor quite interesting.

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References