Case Report

Testicular Yolk Sac Carcinoma in an Aged Sprague-Dawley Rat

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Abstract: A spontaneous yolk sac carcinoma derived from the testis of an old male Sprague-Dawley rat was examined morphologically. The tumor was composed of cuboidal cells arranged into small groups or forming single cell rows. The tumor cells had round to oval, single central or polar nuclei with amphophilic, granular, finely vacuolated cytoplasm. The intercellular spaces contained large amounts of basement-membrane-like, eosinophilic matrix. This matrix was stained positively for laminin and periodic acid-Schiff (PAS). Some visceral cysts were lined with well differentiated cells, flat or cuboidal vacuolated epithelium. An ultrastructural examination showed that the hyaline matrix of the tumor had a fine-lamellar structure. These morphological characteristics in our case strongly suggest that this tumor is a yolk sac carcinoma, being similar to experimentally induced ones. No report of spontaneously occurring yolk sac carcinoma derived from rat testis was found in the literature. (*J Toxicol Pathol* 1998; **11**: 203~204)

Key words: Yolk sac carcinoma, Testis, Spontaneous, Rat

Yolk sac carcinoma, or endodermal sinus tumor, is a rare neoplasm of germ cell origin in mice and rats. Sobis¹ reported one case of spontaneous uterine yolk sac carcinoma in a BB rat. In mice, there are 8 cases of spontaneous tumor in uterus and 16 cases in ovaries in the literature²⁻⁴. This tumor was experimentally induced in uterus by fetectomy, embryo implantation under the kidney capsule, or puncturing the embryos through the uterus wall in female rats and mice⁵⁻¹¹. There have been no reports of both spontaneously occurring or experimentally induced tumor of this kind derived from testis. We found a spontaneous testicular yolk sac carcinoma in an old male rat and described the details of its morphological features.

The animal was an Slc: Sprague-Dawley male rat (SPF, 6 weeks old) purchased from Shizudokyo, Japan. It was housed in a metal cage in an air conditioned animal room controlled at $24 \pm 1^\circ\text{C}$ and $55 \pm 5\%$ relative humidity and maintained on a basal diet (CD-1, Charles River Co., Ltd.) and tap water. Decreased body weight gain was noted from 78 to 86 weeks of age. A $25 \times 23 \times 15$ mm mass was present in the cheek from 97 weeks of age. A pale skin indicative of anemia became evident from 103 weeks of age. The animal showed wasting signs at 106 weeks of age, became moribund, and was killed by deep anesthesia before necropsy. At necropsy, the right testis had a small nodule of $15 \times 8 \times 3$ mm along with a diffuse distribution of tiny yellowish-white foci. The left testis was within normal size and dark red in color. The main organs and tissues taken at necropsy were

fixed in 10% neutral buffered formalin, embedded in paraffin, sectioned at $5 \mu\text{m}$, and stained with hematoxylin and eosin for routine histopathological examination. Cross sections of the testis containing the tumor were stained with periodic acid-Schiff (PAS). Immunohistochemistry was based on the avidin-biotinylated complex (ABC) method for laminin using antisera of anti-rat laminin (Gibco Laboratories Inc., Grand Island, NY, USA). Normal rat yolk sac containing Reichert's membrane was the positive control in the immunohistochemical staining. An electronmicroscope examination was made on a specimen from the paraffin block used for the histopathology.

On microscope, almost all the right testis including the small nodule had been replaced by the tumor structure which was mostly necrotic. The characteristic feature of this tumor was a predominantly eosinophilic hyaline matrix that was intensively positive to the periodic acid-Schiff (PAS) reaction (Fig. 1) and to laminin. The tumor cells were small, uniform in shape, and arranged in clusters, nests, or ribbons in the matrix. Their cytoplasm was amphophilic, finely vacuolated, and granular. Some mitotic and pycnotic figures of nuclei were present. In the necrotic areas of the tumor mass, there were copious hyalinous substances with shadowy cells. Simple small cysts, lined by a flat or cuboidal vacuolated epithelium were rare (Fig. 2). There were no metastatic lesions in the remote organs or tissues. The left testis was replaced by a Leydig cell tumor. The mass in the cheek was diagnosed as Zymbal gland carcinoma and considered to be the cause of anemia. Myeloid hyperplasia in bone marrow and increased extramedullary hematopoiesis in spleen were seen as a secondary hematopoietic reaction to anemia.

On electron microscope, the hyaline matrix of the tumor was composed of a fine-lamellar structure (Fig. 3). Parietal neoplastic cells, which were distinctly bordered by the matrix, had distended cisternae of the rough endoplasmic reticulum, conspicuous vacuoles, and few mitochondria and other

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Fig. 1-A. Yolk sac carcinoma showing tumor cells arranged in clusters, nests, or ribbons. These tumor cells are surrounded by abundant basement membrane hyaline material. HE $\times 60$

Fig. 1-B. The most deeply colored basement membrane consisting of hyaline material surrounds the clusters, nests, and ribbons of tumor cells. PAS $\times 80$

Fig. 2. Simple cyst, lined with flat or cuboidal vacuolated epithelium, suggestive of visceral structures. HE $\times 250$

organelles in the cytoplasm.

Because the character of the present tumor was quite comparable to the spontaneously occurring or experimentally produced yolk sac tumors in rodents, the tumor was diagnosed as a primary testicular yolk sac tumor. Majeed *et al.*³ reported that the rodent yolk sac is composed of visceral and parietal layers that are separated by a thick basement membrane (Reichert's membrane) which are considered to be secreted by the cells of the parietal layer. The present tumor also contained two characteristic morphological features; a hyaline matrix considered to be synthesized by the parietal layers and visceral cysts lined by a cuboidal epithelium.

Sobis¹ reported one case of spontaneous uterine yolk sac carcinoma in a BB rat. Stewart *et al.*² reported 8 cases of spontaneous yolk sac carcinomas in the uterus of mice. Majeed *et al.*³ described 15 ovarian spontaneous yolk sac carcinomas in B6C3F₁ mice in the archives of the National Cancer Institute/National Toxicology Program Carcinogenesis Bioassay Program. Katuta *et al.*⁴ reported one ovarian spontaneous yolk sac carcinoma in a 75-week-old B6C3F₁ female mice. In contrast, there have been many reports on the experimental induction of yolk sac carcinoma

Fig. 3. Note the characteristic laminated appearance of the hyaline material. $\times 17,500$

induced by fetectomy or other surgical procedures in uterus or under the kidney capsule in female rats^{5,9,11}. In humans, this is the most common testicular tumor found in infants and children, constituting about 60% of all testicular tumors¹². To our knowledge, this is the first case of a spontaneous yolk sac tumor occurring in the testis of rats.

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