An Extraskkeletal Osteosarcoma in an Aged Rat

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Extraskkeletal osteosarcomas (ESO) occur rarely in human beings [5]. In animals a few spontaneous cases of ESO have been reported in the dog [1, 4, 6], and guinea pig [2], but no instance of spontaneous ESO has been reported in the rat. In the present report the morphological features of an ESO observed in the thoracic cavity of an aged rat used for life-span observation are described.

A male rat, derived from the Sprague-Dawley strain, 88 weeks of age and 460 g in body weight, was found dead. The animal was born in this laboratory. The usual gross and histopathological examinations were carried out, and ultrastructural examination was conducted on formalin-fixed tumor tissues.

Grayish white multinodular solid masses, 1 to 5

mm in diameter, were found in the pericardium and diaphragm. The pericardium could not be separated from the diaphragm (Fig. 1). Two tumor nodules, about 5 mm in diameter, were observed in the lungs, and one nodule, about 1 mm in diameter, on the epicardium of the left ventricle. No changes suggesting tumorous growth were observed in any other site.

Microscopically osteoid tissue formation was prominent in the tumor tissue in the pericardium, diaphragm, lungs, and heart. Some areas in the osteoid tissues were suggestive of endochondral ossification showing lacunae each containing one to several tumor cells, and other areas contained thick collagen fibers showing intramembranous ossification in the intercellular space. The stromal collagen fibers in the tumor tissue varied in

Fig. 1. Gross appearance showing multinodular masses in the pericardium and diaphragm.

Fig. 2. Prominent osteoid tissue formation. Tumor cells with weakly basophilic cytoplasm (arrow) in the peripheral region in the osteoid. Ossified lesion, lung. HE staining, $\times 340$.

Fig. 3. Deposit of low electron dense amorphous material in the dilatated cisternae of rER is marked in round type tumor cell (left) and spindle type tumor cell (right) is scanty with cytoplasmic organella. Ossified lesion, lung. $\times 5,200$. Bar=5 μm .

Inset: Matrix vesicle-like structure (arrowhead) and deposition of needle crystals of apatite. Ossified lesion, lung. $\times 40,000$. Bar=100 nm.

density from place to place, and cellular components were prominent in the peripheral region of the osteoid tissue.

The tumor cells consisted of round and spindle type cells, both of which had clear nuclei with scanty chromatin and one to two marked nucleoli. The round type cells were rich in weakly basophilic cytoplasm (Fig. 2). The spindle type cells were elongated and poor in cytoplasm. These gross and microscopical findings well corresponded to those described in ESO [3]. No gross abnormality was detected in the skeletal system. Microscopic examination of the femur, sternum, and vertebrae also revealed no change.

Electron microscopically the round type tumor cells had irregularly outlined nuclei with obvious nucleoli and prominent lamellar, vesicular or dilatated rough endoplasmic reticula (rER) in the cytoplasm. Some of these cells contained amorphous materials of low electron density in the dilatated cisternae of the rER. Abundant microfilaments and secretory granules were fre-

quently observed in the cytoplasm. Occasionally the tumor cells had short cytoplasmic projections. The above features of the round type tumor cells with prominent rER indicate their close resemblance to osteoblasts. The spindle type tumor cells had smoothly outlined spheroidal or long spheroidal nuclei with obvious nucleoli and were poor in cytoplasmic organella, microfilaments, and secretory granules. They were thought to be corresponding to tumor cells of osteoblasts in the undifferentiated stage. Depositions of needle crystals of apatite on a matrix vesicle-like structure were noted in the intercellular space. This structure resembled that described in human ESO by Waxman *et al.* [7] (Fig. 3).

The present histopathological and ultrastructural studies revealed that the tumor consisted of various cells representing features of osteoblasts in different developmental stages. Since the tumor formation was confined to the viscera in the thoracic cavity and no abnormality was

observed in any skeletal bone, the present case was diagnosed as an extraskeletal osteosarcoma originating from soft tissues in the thoracic cavity. The tumors in the lungs and the heart were thought to be metastatic ones.

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要 約

老齢ラットの骨外性骨肉腫（短報）：湊 良雄・山村高章・高田 博・小嶋明廣・今泉和則・和田 功・武下政一・岡庭 梓（田辺製薬株式会社安全性研究所）—— 長期飼育したSD系雄ラット（88週齢）の心臓および横隔膜に灰白色結節状で硬い骨様の腫瘤を認めた。腫瘍組織には類骨形成が著明で、rERがよく発達した細胞から、細胞内小器官に乏しい細胞まで、種々の分化段階にある骨芽細胞類似の腫瘍細胞が観察された。間質には基質小胞を中心とする骨化機転も認められた。全身骨格に異常がないことから、本症例は胸腔軟部組織原発の骨外性骨肉腫と診断された。