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Case Report

Rhabdomyosarcoma in the Abdominal Cavity of a 12-Month-Old Female Donryu Rat

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Abstract: Neoplasms of skeletal muscle origin are very rare in the rat. Recently, we experienced a case of rhabdomyosarcoma as a white mass involving the junction of the esophagus and stomach in the abdominal cavity of a 12-month-old female Donryu rat. Histopathologically, the neoplastic cells composing the mass invasively spreaded from the lamina propia to the tunica serosa in the stomach as well as the esophagus. Although the neoplastic cells varied in appearance, pleomorphic atypical cells with abundant eosinophilic cytoplasm were prominent. Some tumor cells were stained blue with phosphotungstic acid hematoxylin. The nuclei of spindle-shaped neoplastic cells were arranged longitudinally like beads. Multinucleate giant cells and mitotic figures were also frequently observed. Immunohistochemically, these neoplastic cells were positive for desmin and myoglobin, whereas they were negative for alpha-smooth muscle actin. Taken together these findings, this tumor was diagnosed as a pleomorphic rhabdomyosarcoma, probably derived from the muscle layer of the lower part of the esophagus. This is the first report of rhabdomyosarcoma in a Donryu rat. (J Toxicol Pathol 2009; **22**: 195–198)

Key words: rhabdomyosarcoma, rat, esophagus

Spontaneous rhabdomyosarcomas are very rare in rats. There are a few reported cases of rhabdomyosarcomas found in the subcutis around the cervical and thoracic regions or the ventral abdominal musculature in young rats[1–3], in the diaphragm of a Wistar rat[4], in the ear[5] and in the uterus[6]. In this article, we report a case of rhabdomyosarcoma found around the junction of the esophagus and stomach in a female Donryu rat at 12 months of age.

A female Donryu (Crj/Donryu, Charles River Japan Inc., Kanagawa, Japan) rat received a single-intrauterine treatment with 100 mg/kg ethylenethiourea at 11 weeks of age and continuous treatments with 70 mg/kg sodium nitrate once a week by gavage to study the effect of sodium nitrate on uterine carcinogenesis. The rat was housed in a plastic cage in an animal room under controlled conditions (temperature of 24 ± 2°C, relative humidity 55 ± 10% and 12-hour light/dark cycle) and fed CRF-1 diet (Oriental Yeast Co., Ltd., Tokyo, Japan) and tap water ad libitum. The animal was euthanized by exsanguination via the abdominal aorta under diethylether anesthesia at 12 months old of age. At necropsy, a white mass approximately 1.5 cm in diameter was observed involving the junction of the esophagus and stomach, but not the diaphragm, in the abdominal cavity. The mass was dissected together with surrounding tissues including the esophagus and stomach and fixed into 10% neutral buffered formalin. After the fixation, these tissues routinely processed, i.e., embedded in paraffin, sectioned at 4 μm and stained with hematoxylin and eosin (HE). Additional histochemical stainings, such as phosphotungstic acid hematoxylin (PTAH) and Masson trichrome staining, and immunohistochemical stainings for desmin (× 50), alpha-smooth muscle actin (α-SMA, × 100) and myoglobin (× 500; Dako Japan, Tokyo, Japan) were performed using serial sections. Animal care and use followed the NIH Guide for the Care and Use of Laboratory Animals.

Histopathologically, the neoplastic cells composing the mass were infiltrating in the lamina propria through the serosa in the esophagus and stomach (Fig. 1a–c). The boundary of the tumor was not clearly demarcated. The composing cells varied in appearance from spindle to pleomorphic, the latter cells being prominent. These cells possessed abundant eosinophilic cytoplasm stained with eosin and Masson trichrome. The nuclei of these neoplastic cells were oval or irregular in shape, and those with bead-like longitudinal arrangement were characteristically noted in the spindle cells. Multinucleated giant cells were also frequently observed (Fig. 1d). There were no clear cross-striations in the tumor cells stained with HE, but a small number of cells stained with PTAH had striation-like structures (Fig. 1e). Frequent mitotic figures were noticed diffusely throughout the neoplastic tissues. In some parts of the tumor tissues, collagen fibers

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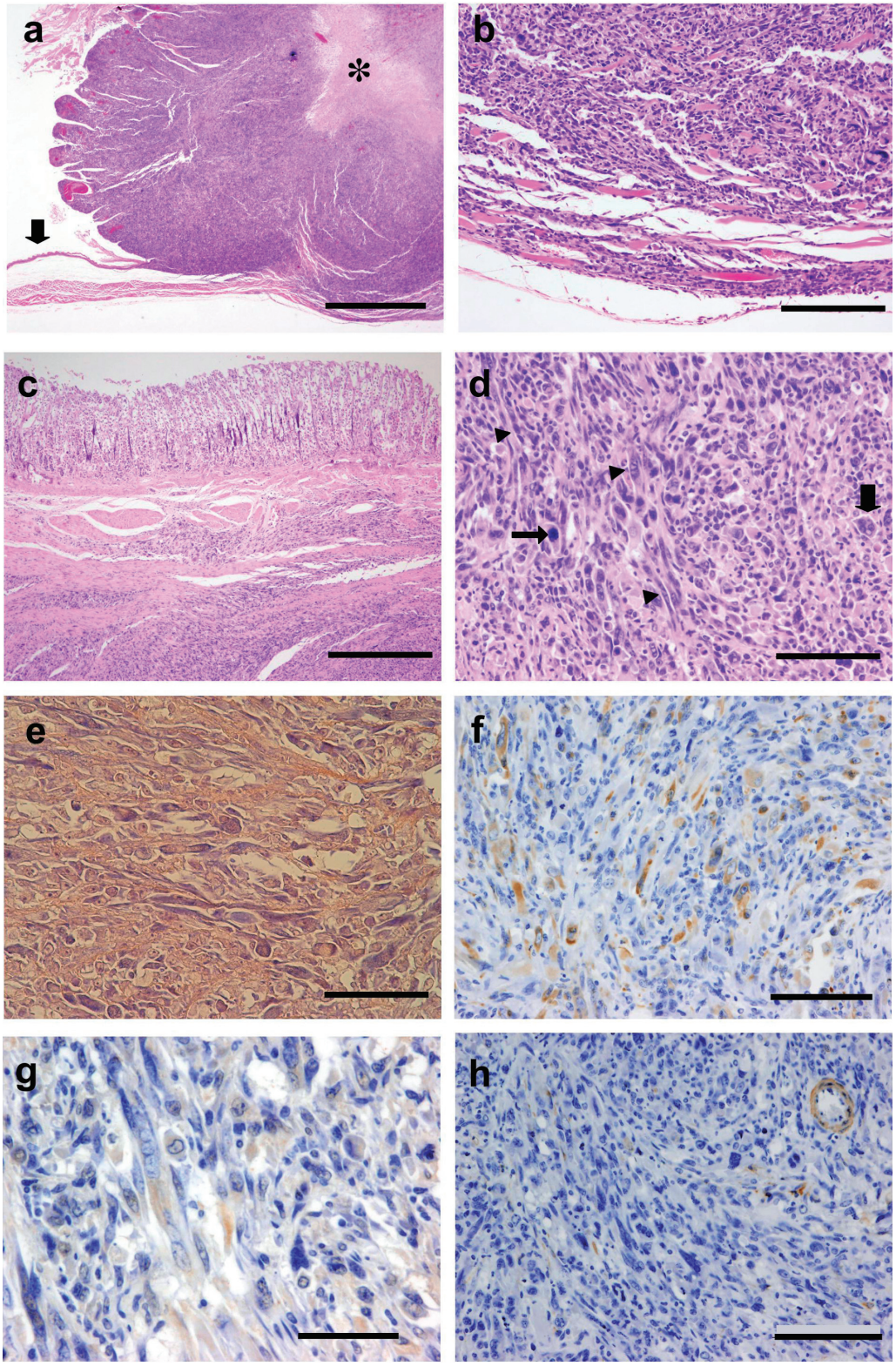

Fig. 1. Histopathological and immunohistochemical findings of rhabdomyosarcoma observed around the junction of the esophagus and stomach of a Donryu rat. Neoplastic cells show invasive growth between the lamina propria and tunica serosa in the esophagus (a and b) and stomach (c). (a) Squamous epithelial cells of the esophagus (arrow). Some necrotic areas (asterisk) can be observed in the tumor tissue. (b) In the muscular layer of the esophagus, some striated muscles are intermingled with neoplastic cells (HE; bars=1 mm, 200 μm and 500 μm for a, b and c, respectively). (d) Neoplastic cells are pleomorphic in appearance, and some nuclei are occasionally arranged like beads in the spindle cells (arrowheads). Multinucleated giant cells (wide arrow) or mitotic figures (thin arrow) are frequently observed within the lesion (HE; bar=100 μm). (e) Some neoplastic cells are stained blue with PTAH (bar=100 μm) and are positive for desmin (f) and myoglobin (g). However, these neoplastic cells are consistently negative for α-SMA (h). Bars= 50 μm (f) and 100 μm (g and h).

were accumulated between neoplastic cells. Although tumor cells were seen within the blood vessel cavity in the muscular layer, metastases to the lung or lymph nodes were not detected. In the tumor tissue, some necrotic areas were also observed. Immunohistochemically, most tumor cells were positive for desmin (Fig. 1f), and some cells were also positive for myoglobin (Fig. 1g), whereas most neoplastic cells were negative for α-SMA (Fig. 1h). In the other organs, there were no histopathological findings except for calcification in the heart, kidneys and stomach. At necropsy, similar tumors were not observed in the other animals of the same treatment group.

Judging from the histopathological and imminohistochemical findings in the present study, this tumor was diagnosed as a pleomorphic rhabdomyosarcoma. The conclusive histopathological findings of this diagnosis were proliferation of various mesenchymal cells and a bead-like arrangement of nuclei, in addition to the results of PTAH- or myoglobin-positive but α-SMA-negative stainability in the neoplastic cells. The origin of this tumor is unclear because of its advanced stage; however, the neoplastic cells intensively invaded into the muscular layer of the esophagus, strongly suggesting that this tumor might have originated from the muscular layer in the lower part of esophagus. This speculation is supported by the fact that the muscular layers of the esophagus in rats consist of striated muscles, whereas those of the stomach are composed of smooth muscles. It is known that the upper part of the muscular layer in the esophagus is also composed of striated muscles in humans. In fact, esophageal rhabdomyosarcomas have been reported as rare in humans[7–10].

Recently, gastrointestinal stromal tumor (GIST) has been identified as a nonepithelial gastrointestinal tumor in animals including dogs, horses and a rat[11–15] as well as humans. GISTs have been suggested to originate from the interstitial cells of Cajal which are characteristically positive for both a proto-oncogenic receptor tyrosine kinase (KIT) and CD34. GISTs are also positive for an undifferentiated mesenchymal antigen, but cases lacking in immunoreactivity with either KIT or CD34[16] or positive for both smooth muscle and neural markers[17] have sometimes been reported. Although GISTs are defined morphologically and immunohistochemically, one human case of GIST showing rhabdomyomatous differentiation occurring in the gallbladder has been reported[18]. However, the diagnosis of the present case was clearly distinguished from GIST due to the conclusive histological, histopathological and immunohistochemical findings described above.

The tumor in the present case was detected in one animal only of an ethylenethiourea and sodium nitrate-treated group of rats. Therefore, this tumor may have been incidental and might not have been related to these treatments. This is the first report of rhabdomyosarcoma in a Donryu rat.

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