Case Report

Retroperitoneal Fibromatosis in a Cynomolgus Monkey (Macaca fascicularis)

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Abstract: A palpable abdominal mass was found in a 4-year-old female cynomolgus monkey (Macaca fascicularis) with chronic anorexia. Grossly, there were numerous coalescing firm nodular lesions, 1 to 5 cm, scattered in the omentum and mesentery. Histologically, there was prominent infiltrative growth of fibroblastic cells with a large amount of collagen fibers in the nodular lesions involving the intestinal tract. The morphological features of the lesion were similar to those of retroperitoneal fibromatosis (RF) in SRV-2-infected macaques, and also closely resembled those of peritoneal desmoid tumor in human. This macaque case is possibly the first reported case of RF in Japan.

Key words: retroperitoneal fibromatosis, cynomolgus monkey, Macaca fascicularis

Humans and nonhuman primates are genetically close and have common features in anatomical and physiological aspects. As for proliferative lesions, although nonhuman primates show a sharply lower incidence than those of equivalent proliferative lesions in humans, their morphological features closely resemble those that occur in humans.

A 4-year-old female cynomolgus monkey (Macaca fascicularis), which was bred and reared in a breeding colony, was obtained from a commercial supplier, and was placed in a quarantine room in the laboratories at Sankyo Co. Ltd. By a physiological examination performed during the quarantine period, a palpable mass was found in the abdominal cavity. The animal was removed from experimental use, and was euthanized humanely by blood exsanguination under deep anesthesia. Monkeys in the facility were housed individually in stainless steel cages in a relatively isolated room maintained at a temperature of 25º C. They were fed a commercial primate diet (Purina Monkey Chow, Ralston Purina Co., Saint Louis, MO), apples, bananas, and oranges. Water was freely provided with an automatic watering system.

A complete necropsy was done immediately after death. The abdominal lesions, lungs, liver, spleen, lymph nodes, kidneys, urinary bladder, adrenals, thyroids, salivary glands, stomach, small intestines, large intestines, pancreas, and skeletal muscle were collected and fixed in 10% buffered formalin. After fixation, the tissue blocks were dehydrated and embedded in paraffin wax in the usual manner, sectioned (5 µm) and stained with haematoxylin and eosin (HE). Selected sections of the intestinal tracts containing nodular lesions were stained with periodic acid-Schiff (PAS), Masson’s trichrome, Alcian blue, silver impregnation, and Sudan III stains. For immunohistochemistry, the labeled streptavidin-biotin (LSAB) method was applied using commercial kits (Dako Corp., Santa Barbara, CA). The primary antibodies used were anti-vimentin, cytokeratin, S-100, myosin, myoglobin, and alpha-anti-trypsin (Dako Corp., Santa Barbara, CA). For electron microscopy, small pieces of formalin-fixed tissues from a mesenteric lesion were post-fixed in 2% phosphate-buffered glutaraldehyde and 1% osmium tetroxide and routinely processed for epon embedding. Ultra-thin sections were stained with uranyl acetate and lead citrate, and examined with a transmission electron microscope (Hitachi; H-800, Japan).

Grossly, there were multifocal, coalescing yellowish-white firm masses, 0.5 to 5 cm in size each, in the omentum and ileocecal mesentery (Fig. 1). On the surface of the liver, there were several small masses implanted in the capsule. The mesenteric lymph nodes were small, and were involved in the mesenteric mass. The inguinal and maxillary lymph
Fig. 1. Yellowish white firm tumor nodules in the omentum (O) and mesentry (M). Formalin-fixed tissue.

Fig. 2. Infiltrative growth of fibroblastic cells with collagen production from the subserosa (S) to muscle layer (M) in the large intestine. HE stain. Bar = 430 µm.
Fig. 3. Highly cellular region in the periphery of the nodule. HE stain. Bar = 50 µm.

Fig. 4. A: A large amount of collagen fibers among fibroblastic cells in the central part of the tumor nodule. HE stain. Bar = 50 µm. B: Masson’s trichrome stain. The bundle of collagen fibers was dark blue. Bar = 36 µm. C: Proliferating fibroblastic cells are intensely positive for vimentin. Labeled streptavidin-biotin (LSAB) method. Bar = 18 µm.
nodes were also small in size.

Histopathologically, there was prominent infiltrative growth of fibroblastic cells with a large amount of collagen fibers in the abdominal nodular masses (Fig. 2). The cellularity of the proliferating fibroblasts and amounts of collagen fibers varied in part of nodular lesions. The periphery of the nodules was moderately to highly cellular, with a slight to moderate cell atypia represented by larger oval nuclei and prominent nucleoli (Fig. 3). Mitotic figures were rare in the nodular lesions. In comparison, in the central part of the nodules, there were fewer fibroblastic cells, but those existing were well-differentiated, longer and thinner, and spindle-like in appearance, with a large amount of collagen production (Fig. 4A). For the most part, the fine collagen fibers were arranged densely, with a wavy appearance, but there were frequent acidophilic homogenous areas with a hyaline-like appearance. In the intestinal wall, there was prominent infiltration of fibroblastic cells from the serosa to the smooth muscle layers, frequently extending into the submucosa area. The liver revealed marked infiltrative growth of fibroblastic cells with marked production of collagen fibers like in the mesenteric nodules, through the capsule to the liver parenchyma. Masson’s trichrome staining revealed a large amount of blue fibers compatible to collagen among fibroblastic cells (Fig. 4B), and the lesions were moderately positive with Alcian blue stain. The silver impregnation stain revealed the presence of a small amount of reticulum fibers in the lesion. The PAS reaction and Sudan III stain were negative.

Immunohistochemically, the proliferating cells were intensely positive for vimentin (Fig. 4C), and negative for cytokeratin, S-100, myosin, myoglobin and alpha-antitrypsin.

By electron microscopy, numerous bundles of collagen fibrils with regular alternating dark and light bands (Type 1 collagen) were seen. The fibroblastic cells were not well-preserved to detect viral particles in the cytoplasm.

In extra-abdominal organs, there was a slight to moderate atrophy of lymphoid follicles in the spleen and lymph nodes. Occasional balantidium spp. were observed in the lumen of the colon.

Based on the characteristic infiltrative growth of fibroblastic cells with a large amount of collagen production, the present case was diagnosed as retroperitoneal fibromatosis (RF). In macaques, mesenchymal proliferative disease known as localized retroperitoneal fibromatosis (RF)4–7. RF has been reported in approximately 25% of the deaths that occurred in a colony of pigtailed macaques (Macaca nemestrina) in which type D simian retro virus (SRV-2) infection was common at the Regional Primate Center and are possibly unrelated to RF. The fibromatosis is divided into two major clinicopathologic groups: the superficial fibromatosis and the deep fibromatosis. The deep fibromatosis includes so-called desmoid tumors that arise in the abdomen and muscle of the trunk. Compared with the superficial lesions, they are characterized by a greater tendency to recur and grow in a locally aggressive manner. The morphological features of the present case closely resembled desmoid type of fibromatosis in human female patients based on the site of occurrence and morphology, which occasionally occur in the abdomen in women in close association with pregnancy2. The pathogenesis of desmoid tumor is still undetermined, although excessive contraction of muscle and affection of hormonal disorder are considered to be causes.

As differential diagnoses, other soft tissue neoplasms2 such as fibroma, fibrosarcoma, leiomyosarcoma, and mesothelioma were considered. Fibroma is a benign fibroblastic neoplasm with prominent collagen production, but it is well demarcated and shows no infiltrative growth. Fibrosarcoma has more prominent cell atypia and cellularity, and produces fewer collagen fibers than fibromatosis. It can be easily differentiated from leiomyosarcoma according to the shape and arrangement of the nuclei, and to the amount of collagen production. Mesothelioma occurs from the serosa of the thoracic or abdominal cavities. It was necessary to differentiate between the present case and the sarcoma type of mesothelioma, which shows morphological variation consisting of an admix of epithelial glandular and sarcomatous components. The present case consisted only of fibroblastic cells and collagen, which was an important point in differentiating the two.

There was occasional balantidium spp. infection in the lumen of the colon, these being one of the common parasites in the macaque, and which are found only in the intestinal tract and are possibly unrelated to RF.

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References


