Neuroendocrine Tumor in the Lung of a Captive Black Spider Monkey (Ateles paniscus)

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ABSTRACT. This paper describes a neuroendocrine (NE) tumor of the lung that was observed during the necropsy of a 14-year-old female black spider monkey (Ateles paniscus) with sudden death. Grossly, multifocal firm and coalescing nodular masses were observed in the lung. The histological examination showed the tumor to be an NE tumor with polygonal cells grouped in small solid aggregates, with regularly sized, spherical, centrally placed nuclei with modest, lightly granular cytoplasm suspended in a fibrovascular stroma. The immunohistochemical examination revealed the tumor to be positive for cytokeratin, chromogranin A and synaptophysin, and negative for CD56. To the best of our knowledge, this is the first report of NE tumor in the lung of the black spider monkey.

KEY WORDS: black spider monkey, carcinoid, neuroendocrine tumor.

Neuroendocrine (NE) tumor (so-called carcinoid tumor) is derived from enterochromaffin or Kulchitsky cells, which are widely distributed in the body of animals and humans. For this reason, they can be found at almost any location in the body but generally originate from the foregut, midgut, and hindgut [7, 8, 16]. In humans, the incidence of NE tumors is approximately 2.5 per 100,000 people per year [9]. NE tumors in animals have been reported in both domestic and wild species. There are many reports of NE tumors in dogs, affecting the different organ systems including the small and large intestines, stomach, lung and liver [7]. NE tumors have also been observed in various organs of wild animals such as liver of an elephant [15], duodenum of a cynomolgus monkey (Macaca fascicularis) [6] and in lung of a hooded seal (Cystophora cristata) [1]. However, to the best of our knowledge, there are no reports of NE tumors of the lung in any monkey species. Therefore, this study describes the histopathological and immunohistochemical features of a NE tumor of the lung in a captive black spider monkey (Ateles paniscus).

A 14-year-old female black spider monkey from a zoo in Gyeonggi Province, Republic of South Korea died suddenly. A gross examination revealed prominent lesions in the lung; Multifocal coalescing pulmonary nodular masses (average 2.0 × 1.5 × 1.0 cm) with a minimally raised contour, an umbilical appearance of some nodules and a poorly demarcated border similar to an abscess (Fig. 1). The largest mass measured 8.0 × 4.0 × 3.0 cm in the ventral portion of the right diaphragmatic lobe. The mass was found to be firm on incision. The other significant gross lesions were diffuse gastritis with ulcer and hemorrhages. Likewise, the small intestines and some portions of the large intestines also contained some mucosal hemorrhages. There were no visible lesions in any of the other organs including the liver, kidneys, spleen, urinary bladder, heart and brain. The tumor masses appeared to be confined only in the lung, as no metastatic focus was observed in any organs.

A routine histopathological examination using hematoxylin and eosin staining was performed upon the collected tissue samples from the tumor masses and other organs. Serial sections from the neoplasm were examined immunohistochemically using the avidin-biotin-peroxidase complex (ABC) procedure (Vectastain Elite ABC Kit; Vector Laboratories, Burlingame, CA, U.S.A.) [4]. Mouse monoclonal antibodies against chromogranin A (CGA, 1:500, Dakocytomation, Glostrup, Denmark), synaptophysin (SYG, 1:100, Dakocytomation), CD56 (neural cell adhesion molecule, 1:200, Dakocytomation,) and cytokeratin (CK, prediluted, Vector Laboratories, Burlingame, CA, U.S.A.) were used as primary antibodies. The endogenous peroxidase activity in the deparaffinized tissue samples from the tumor masses and other organs. Serial sections from the neoplasm were examined immunohistochemically using the avidin-biotin-peroxidase complex (ABC) procedure (Vectastain Elite ABC Kit; Vector Laboratories, Burlingame, CA, U.S.A.) [4]. Mouse monoclonal antibodies against chromogranin A (CGA, 1:500, Dakocyтомation, Glostrup, Denmark), synaptophysin (SYG, 1:100, Dakocyтомation), CD56 (neural cell adhesion molecule, 1:200, Dakocyтомation,) and cytokeratin (CK, prediluted product, Dakocyтомation) were used as primary antibodies. The endogenous peroxidase activity in the deparaffinized sections was blocked using 3% H2O2 for 10 min. The sections were incubated with any of the primary antibodies at 4°C for 16 hr, then with the biotinylated secondary antibody (anti-mouse IgG, Vector Laboratories, Burlingame, CA, U.S.A.) for 30 min at room temperature, and further with the avidin-peroxidase conjugate (Vector Laboratories, Burlingame, CA, U.S.A.) for 30 min respectively. Staining was developed in a 0.05% 3,3'-diaminobenzidine solution. The appropriate positive and negative controls were performed. In the negative control, the primary antibody was replaced by normal serum.

Microscopically, the tumor cells did not occupy the airway tubular passages but were found in the alveolar parenchyma. Round to ovoid tumor cells were observed with a solid nested pattern within a thin fibrovascular stroma. A ribbon or festoon-like pattern was observed at the periphery...
Fig. 1. Lung of a black spider monkey. Multifocal coalescing pulmonary nodular masses (arrows), minimally raised contour, umbilical appearance. Bar=2 cm.

Fig. 2. Lung. Typical neuroendocrine tumor contains neoplastic cells with regularly sized, spherical, centrally placed nuclei and finely nuclear chromatin containing modest, granular cytoplasm. HE. Bar=200 µm.

Fig. 3. Positive immunoreaction of tumor cells for cytokeratin. Avidin-biotin-peroxidase complex method. Bar=50 µm.

Fig. 4. Positive immunoreaction of tumor cells for chromogranin A. Avidin-biotin-peroxidase complex method. Bar=50 µm.

Fig. 5. Positive immunoreaction of tumor cells for synaptophysin. Avidin-biotin-peroxidase complex method. Bar=50 µm.
of the mass. The tumor cell contained regularly sized, spherical and centrally placed nucleus with fine nuclear chromatin, and lightly granular cytoplasm (Fig. 2). There were few areas of necrosis and mitotic figures. Immunohistochemically, the tumor cells were positive for CK (Fig. 3), CGA (Fig. 4) and SYP (Fig. 5), and negative for CD56 (data not shown). This tumor was, therefore, diagnosed as a typical NE tumor in the lung.

NE cells are widely distributed in various tissues, such as the tracheobronchial tree, liver, pancreas and genitourinary system. In human medicine, NE tumors (carcinoid tumors) have been found in a wide range of organs with the gastrointestinal and pulmonary tracts being the most common sites [14]. On the contrary, in veterinary medicine, there are some reports on the occurrence of NE tumors mainly in the gastrointestinal tract [2, 3, 8, 9]. In human medicine, the pathological classification of NE tumors and other endocrine neoplasms is quite detailed: typical carcinoid tumor, atypical carcinoid tumor, large cell neuroendocrine carcinoma, non-small cell carcinoma with neuroendocrine features and small cell carcinoma [10]. Immunohistochemical staining of the present tumor mass helped the differentiation of this tumor from large cell NE carcinomas, non-small cell carcinomas with NE features and small cell carcinomas in both human patients and animals [12]. The differentiation between typical and atypical carcinoid tumors is based mainly on the mitotic count. Typical NE tumors have less than two mitoses per square millimeter on the section and a lack of necrosis. Atypical carcinoids either have 2 to 10 mitoses per square millimeter or contain foci of necrosis, or both. The necrosis is more or less punctuate [13]. Using such human oncology classification, the present tumor was classified as a typical carcinoid tumor of the lung based on its specific histopathological features and immunohistochemical reactions. A similar histological description of a NE tumor has been reported in dogs [5, 12]. We observed faint staining of granules while NE tumors with dark fine cytogranules were reported earlier in dogs [11]. Ultrastructural study reveled that in all granules cores were separated from outer limiting membrane by narrow electron lucent halo and cells had a well developed paranuclear golgi appratus and numerous randomly scattered tonofilament bundles [12]. The immunohistochemical results in the present case are in agreement with the previous cases. The incidence of primary lung NE tumors in animals is unknown but is assumed to be very low. Most primary tumors in the lung are adenocarcinomas and alveolar carcinomas. NE tumors in animal lung are occasionally reported [1, 5, 11].

In the present monkey case, no hematological and serum biochemical examination was carried out due to absence of clinical signs. It is believed that the most likely cause of death was a stomach ulcer leading to the internal hemorrhages. The presence of the tumor in the lung was not direct cause of death as it was not interfering with the air passages. In human cases also no carcinoid tumor in the lung results in the death of the patient. This is the first report of the NE tumor in a black spider monkey. This case is important because of an animal disease model with the similarity of lesions in human lung carcinomas. The long life span of non-human primates due to captivity and the close phylogenetic relationship with humans may be intriguing feature of the present case as a model of human cancers.

REFERENCES