



Case Report

Lung adenocarcinoma and splenic histiocytic sarcoma in an African pygmy hedgehog (*Atelerix albiventris*)

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Abstract

The African pygmy hedgehog is increasingly being kept as a pet, and studies regarding the primary diseases that affect this species are essential for advancing medicine in these animals. This report aims to describe a case of an adult male hedgehog living in captivity. The hedgehog presented progressive weight loss and lethargy. An abdominal ultrasound examination was performed, revealing a splenic mass. Therefore, symptomatic treatment was chosen. After three months, with no clinical improvement, the animal was euthanized. The cadaver underwent necropsy, and histopathological evaluation with Hematoxylin and Eosin staining revealed two distinct neoplasms in different organs: pulmonary adenocarcinoma and round cell neoplasm in the spleen. Additionally, non-neoplastic lesions were observed in other organs. The splenic tissue was subjected to an immunohistochemical diagnostic panel using IBA1, CD3, PAX5, MUM1, and AE1/AE3 markers. Positive staining for IBA1 was observed, favoring the diagnosis of histiocytic sarcoma. We emphasize the importance of preventive veterinary medicine in assessing these animals' health status and detecting possible neoplastic processes. Tumors are commonly described in this species, and clinical signs usually are nonspecific, leading to the animal's death or euthanasia.

Keywords: four-toed hedgehog, Erinaceidae, pathology, neoplasia, immunohistochemistry.

Introduction

The African hedgehog (*Atelerix albiventris*), the four-toed hedgehog, belongs to the Erinaceidae family and is a small nocturnal mammal found in West, Central, and East Africa. It can be seen in grasslands, shrubs, savannas, and suburban gardens, living in burrows. Their diet consists of invertebrates such as earthworms, slugs, and snails. The animals have recently become popular as exotic pets worldwide and are commonly kept in zoological parks (2, 14).

Several studies on the incidence of diseases in these animals have been published, with neoplastic processes widely described (6, 4, 10, 12, 16). In the study conducted by Okada *et al.* (2018), which evaluated the presence of diseases in African Hedgehogs between the years 2012 to 2017, neoplastic lesions were observed in 60% of cases, and 74.6% of tumors were

classified as malignant. Generally, the systems most affected by neoplasms in this species are the integumentary, digestive, endocrine, hemolymphatic, and reproductive systems (14, 15).

The Gardhouse and Eshar (4) study identified neoplasms as the third most frequent pathological finding in hedgehogs. They were observed in 20.7% (22/106) of the animals examined, with squamous cell carcinoma in the oral cavity being the predominant type of neoplasm, accounting for 10 out of the 12 neoplasms verified.

According to the literature consulted, lymphoma is one of the most frequently diagnosed neoplasms among hematopoietic tumors in hedgehogs (5, 16). Additionally, there have been an increasing number of reported cases of histiocytic sarcoma (10, 11, 17). In the Son *et al.* (17) study, histiocytic sarcomas diagnosed in 8 animals of this species showed aggressive behavior. These sarcomas were classified

as either localized, with a primary origin in the spleen or skin, or disseminated, with a large mass in the large intestine and smaller nodules in organs such as the liver, spleen, and kidney.

In veterinary medicine, primary pulmonary neoplasms are rarely described, with a frequency ranging from 0.1% (9) to 0.9% (18) in dogs, which are the most affected species. Among dogs, adenocarcinomas are the most prevalent type of lung tissue tumor (21). However, in the case of African Hedgehogs, pulmonary adenocarcinoma is rarely reported, with previous mentions in two studies (13, 16).

This case report presents the gross, microscopic, and immunohistochemical findings of lung adenocarcinoma and histiocytic sarcoma in the spleen of an African hedgehog.

Case description

An adult male hedgehog (*Atelerix albiventris*) was voluntarily delivered by its former owner to Associação Mata Ciliar (AMC), located in the municipality of Jundiá, State of São Paulo, on February 24th, 2022. At AMC, the hedgehog was fed cat food daily and received mealworm larvae (*Tenebrio molitor* and *Zophobas morio*) twice a week. In August of the same year, the animal started exhibiting lethargy and experiencing

progressive weight loss. An ultrasound examination revealed a rounded, hypoechoic, and heterogeneous splenic mass with undefined borders, measuring 2.31 x 1.84 cm. Symptomatic treatment was administered for three months; however, due to the poor prognosis, euthanasia was chosen.

The cadaver underwent a necropsy examination, which revealed no external abnormalities. During the internal evaluation, it was observed that a specific area of the spleen exhibited a mass consisting of multiple nodules. The mass had an overall size of 4.5 cm x 2.7 cm x 2.0 cm. It exhibited a firm consistency and a predominantly white color with reddish areas interspersed (Fig. 1A). When the affected area was cut, the coloration remained the same, the surface appeared irregular, and there was no drainage of bloody fluid. (Fig. 1B). The lungs showed slightly distended lobes containing solid, yellowish nodular formations distributed in a multifocal pattern, measuring approximately 0.3 cm x 0.2 cm (Fig. 1C). One of the kidneys displayed reduced size and, upon cutting, exhibited paleness, decreased cortical-medullary definition, cystic formations in the cortical layer, and hydronephrosis (Fig. 1D).

Several tissues were collected, fixed in a 10% phosphate-buffered formalin solution (pH 7.4), and processed according to the standard protocol. The tissues were embedded in paraffin, cut into 5µm sections, and stained with hematoxylin

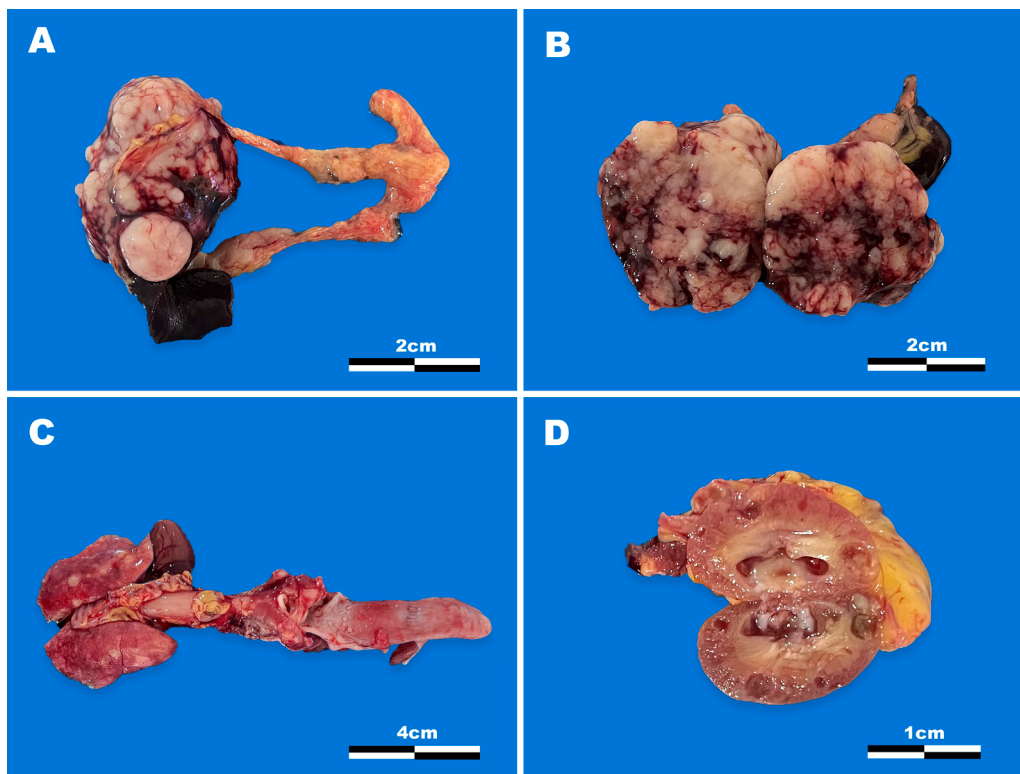


Figure 1. Postmortem examination of an adult male African pygmy hedgehog (*Atelerix albiventris*). **A-** Spleen with rounded mass containing multiple whitish nodules amid reddish areas. **B-** When cutting the splenic mass, note the irregular surface and predominantly whitish color. **C-** Lung containing yellowish and multifocal solid nodular formations. **D-** Kidney with reduced size, showing pallor, decreased cortical-medullary definition, cystic formations in the cortical layer, and hydronephrosis.

and eosin (H&E). For the immunohistochemical test, tissue sections were also processed for histology, embedded in paraffin, and placed on silanized slides. Antigen retrieval was performed using the moist heat method in a steam pan for 20 to 30 minutes. Primary antibodies were incubated for 18 hours at 4°C. The Advance system was used as the secondary antibody. Staining was performed using 3,3-diaminobenzidine, followed by counterstaining with Harris hematoxylin.

Histopathological evaluation using H&E staining revealed the presence of a malignant neoplastic proliferation of epithelial cells within the lung tissue. The cells exhibited a marked cellularity and displayed an infiltrative growth pattern with poor delimitation and no encapsulation. The cells were columnar and arranged in papillae, surrounded by a discrete fibrovascular stroma. Individually, the cells had indistinct shapes and borders, and their cytoplasm appeared moderate and eosinophilic. The nuclei were hypochromatic and round, containing finely grouped chromatin and occasionally prominent single nucleoli. Marked anisocytosis and anisokaryosis were observed,

as well as 3 figures of mitosis (2.37 mm²; Figs. 2A and 2B). Based on this analysis, the diagnosis of pulmonary papillary adenocarcinoma was performed in the animal.

The renal histopathological evaluation revealed the presence of severe glomerular proteinosis and glomerulosclerosis, accompanied by lymphocytic interstitial nephritis and necrosis (Figs. 3A and 3B).

In the spleen, the microscopic evaluation demonstrated a neoplastic proliferation of round cells characterized by high cellularity and an infiltrative growth pattern. The cells were arranged in a solid pattern within a discrete fibrocollagenous stroma. Individually, the cells exhibited abundant eosinophilic cytoplasm and rounded, hypochromatic nuclei containing finely grouped chromatin and distinct single nucleoli. Moderate anisocytosis and anisokaryosis were observed, as well as five figures of mitosis (2.37 mm²; Fig. 4A). Additionally, extramedullary hematopoiesis was present, marked by the abundant presence of megakaryocytes (Fig. 4B). The H&E evaluation of the other tissues did not reveal any microscopic alterations.

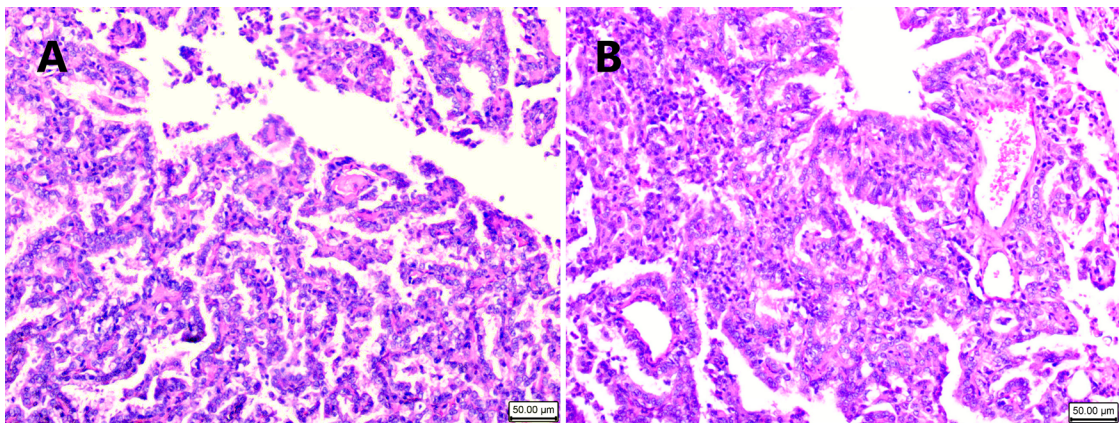


Figure 2. Histopathological evaluation of the lung from an adult male African pygmy hedgehog (*Atelerix albiventris*). **A-** and **B-** Pulmonary adenocarcinoma. The neoplastic epithelial cells exhibited a papillary pattern. HE, bar=50µm.

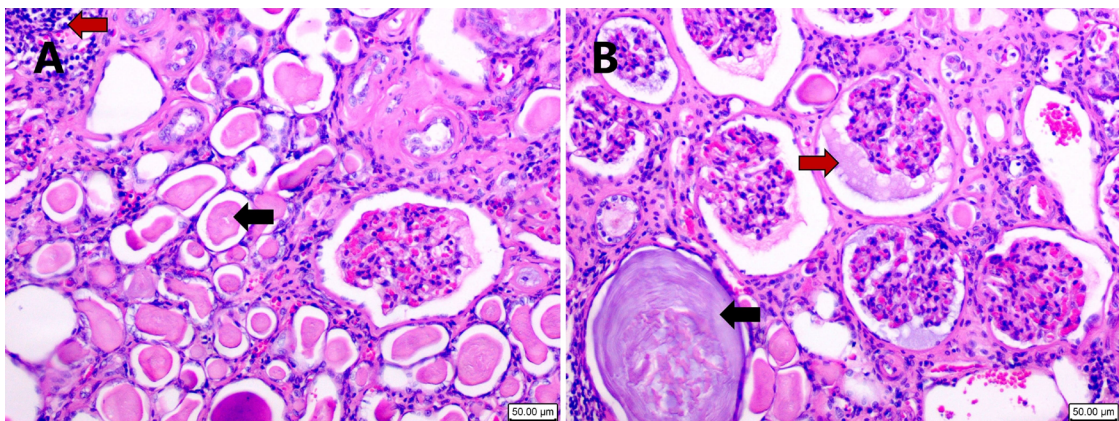


Figure 3. Histopathological evaluation of the kidney from an adult male African pygmy hedgehog (*Atelerix albiventris*). **A-** Hyaline casts in the lumen of renal tubules (black arrow) and interstitial nephritis with predominantly lymphocytic inflammatory infiltrate (red arrow). HE, bar = 50µm. **B-** Glomerular fibrosis (glomerulosclerosis) (black arrow) and glomerular edema (red arrow). HE, bar = 50µm.

An immunohistochemical technique (IHC) was employed to further elucidate the splenic neoplastic process. The IHC analysis revealed that the neoplastic cells expressed IBA1 (Fig. 4C) but did not exhibit expression of CD3, PAX5, MUM1, and AE1/AE3. Additionally, positive Ki67 staining was observed in approximately 30% of neoplastic cells. Consequently, the immunohistochemical findings and the morphological profile substantiate the diagnosis of histiocytic sarcoma.

Discussion

Retrospective studies on pathological findings in hedgehogs suggest that the increase in life expectancy associated with captivity may result in a higher occurrence of tumors in these animals, particularly affecting adult individuals with an average age ranging from 3 to 5 years (13, 14). In the present study, the hedgehog under investigation was also an adult and had been kept in captivity for an extended period. The diagnosis revealed two distinct tumor processes: a pulmonary adenocarcinoma, which is rarely reported in this species, and a splenic histiocytic sarcoma, a neoplasm that has been frequently documented in hedgehogs (10, 11, 17).

Histiocytic sarcoma is a neoplasm composed of round cells and primarily arises from cells exhibiting morphological and immunohistochemical characteristics of dendritic cells or macrophages. It can manifest as a localized tumor originating from a single tissue or organ, with solitary or multiple foci, or as a disseminated condition, spreading to lymph nodes and other tissues (1, 7). Histiocytic sarcoma is a rare neoplasm in dogs that can occur in any tissue and exhibit rapid metastasis (7, 19). Its incidence is even lower in cats than in dogs (3). Histiocytic sarcoma is sporadic in humans and represents less than 1% of hematopoietic tumors. Clinical signs in dogs are nonspecific, including weight loss,

lethargy, and anorexia (8). In the case of the hedgehog examined in this study, the clinical signs mentioned above persisted despite having two distinct tumor processes.

In African pygmy hedgehogs, histiocytic sarcoma has been previously reported in localized forms, affecting the spleen, skin, and nervous system (11, 17), as well as in disseminated forms, involving multiple tissues such as the liver, kidney, spleen, lung, heart, bone marrow, uterus, gallbladder, thymus, adrenal, mesenteric lymph nodes, intestine, mesentery, and stomach (10, 17). In the current case, the histiocytic sarcoma was localized in the spleen of a male hedgehog, as detected by abdominal ultrasound. Similarly, in a study conducted by Son et al. (17), the same tumor was observed in the spleen of a female hedgehog using the same examination. The histopathological characteristics of the tumor were equivalent, and immunohistochemical staining also showed positive results for IBA-1. It is worth noting that IBA-1 was the most significant marker, with a higher percentage of positive cells (76 to 100%) in the study by Son et al. (17). The anti-Iba-1 antibody is used to identify macrophages and monocytes in the immunohistochemical diagnosis of proliferative histiocytic disorders in dogs (7).

In dogs and hedgehogs, histiocytic sarcoma is an aggressive neoplasm with a poor prognosis. Treatment options, such as chemotherapy and surgical excision, have demonstrated the ability to enhance the life expectancy of dogs diagnosed with this tumor compared to those who receive symptomatic or no treatment (19). Surgical excision of localized forms of histiocytic sarcoma may lead to a cure for the animal, although metastasis can occur early in the disease (20). In this study's case of the hedgehog, metastasis was not observed, even after three months of detecting the splenic mass through abdominal ultrasound. Furthermore, the histopathological evaluation of the tissues revealed no metastasis signs. Therefore, it was possible to consider performing a surgical excision of this mass, which could have increased

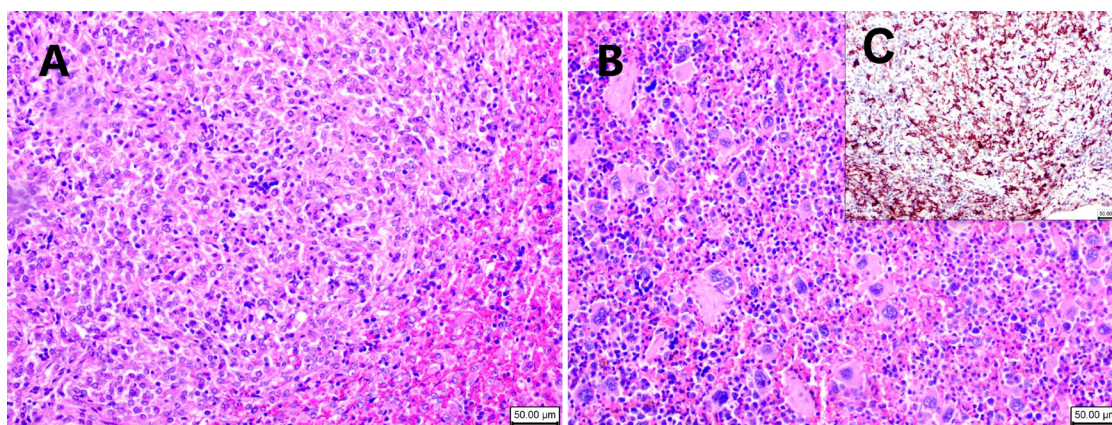


Figure 4. Histopathological evaluation of the spleen from an adult male African pygmy hedgehog (*Atelerix albiventris*). **A-** Histological features of hedgehog histiocytic sarcoma. Note that the cells have a rounded nucleus, finely grouped chromatin, and abundant eosinophilic cytoplasm - moderate anisokaryosis and anisocytosis. HE, bar = 50µm. **B-** Note extramedullary hematopoiesis (black arrow). HE, bar = 50µm. **C-** Immunohistochemical features of hedgehog histiocytic sarcoma. Neoplastic cells are positive for IBA-1. Bar = 50µm.

the animal's survival time. However, the development of a separate and distinct tumor process, a papillary pulmonary adenocarcinoma, was diagnosed solely through histopathological examination, further complicating the hedgehog's chances of survival.

Pulmonary adenocarcinoma has been previously described in African pygmy hedgehogs (13, 16). However, primary pulmonary neoplasms are considered rare in this species, as well as in dogs. The Veterinary Cooperative Oncology Group conducted studies that evaluated the main clinical signs of lung carcinoma in dogs, which include cough as the primary sign, followed by dyspnea and lethargy. It is worth mentioning that 25% of the animals did not exhibit respiratory clinical signs before diagnosis (21). In this study's case of the hedgehog, no respiratory signs were observed, only lethargy and weight loss.

In conclusion, this is the first documented case of a hedgehog experiencing both histiocytic sarcoma and papillary lung adenocarcinoma simultaneously, resulting in lethargy and progressive weight loss. Preventive veterinary medicine, including hematological and biochemical tests, radiographs to detect metastasis, and abdominal ultrasounds can aid in diagnosing and suspecting neoplastic processes. Hedgehogs are commonly diagnosed with tumors; sometimes, the clinical signs can be nonspecific. If the neoplasm is not promptly detected and treated, the prognosis worsens, ultimately leading to the animal's death.

Conflict of Interest

The authors declare no competing interests.

References

- Affolter VK, Moore PF. Localized and disseminated histiocytic sarcoma of dendritic cell origin in dogs. *Vet Pathol*. 2002;39(1):74-83.
- Cassola, F. 2016. *Atelerix albiventris* (errata version published in 2017). The IUCN Red List of Threatened Species 2016: e.T40602A115174097. <https://dx.doi.org/10.2305/IUCN.UK.2016-3.RLTS.T40602A22324217.en>. Accessed on 27 June 2023.
- Friedrichs KR, Young KM. Histiocytic sarcoma of macrophage origin in a cat: case report with a literature review of feline histiocytic malignancies and comparison with canine hemophagocytic histiocytic sarcoma. *Vet Clin Pathol*. 2008;37(1):121-8.
- Gardhouse S, Eshar D. Retrospective study of disease occurrence in captive African Pygmy hedgehogs (*Atelerix albiventris*). *Isr J Vet Med*. 2015;70(1):32-6.
- Heatley JJ. Hedgehogs. In: Mitchell MA, Tully TN, editors. *Manual of Exotic Pet Practice*. St. Louis: Saunders Elsevier; 2009. p. 433-55.
- Mikaelian I, Reavill DR. Spontaneous proliferative lesions and tumors of the uterus of captive African hedgehogs (*Atelerix albiventris*). *J Zoo Wildl Med*. 2004;35(2):216-20.
- Moore PF. A review of histiocytic diseases of dogs and cats. *Vet Pathol*. 2014;51(1):167-84.
- Moore PF. Canine and Feline Histiocytic Diseases. In: Meuten DJ, editor. *Tumors in Domestic Animals*. 5th ed. Ames: Wiley Blackwell; 2017. p. 322-36.
- Nielsen W. Comparative pathology of pulmonary disease. In: Liebow AA, Smith DE, editors. *The Lung*. Baltimore: Williams and Wilkins; 1968. p.226-44.
- Ogihara K, Itoh T, Mizuno Y, Tamukai K, Madarame H. Disseminated Histiocytic Sarcoma in an African Hedgehog (*Atelerix albiventris*). *J Comp Pathol*. 2016;155(4):361-364.
- Ogihara K, Suzuki K, Madarame H. Primary Histiocytic Sarcoma of the Brain in an African Hedgehog (*Atelerix albiventris*). *J Comp Pathol*. 2017;157(4):241-5.
- Okada K, Kondo H, Sumi A, Kagawa Y. A retrospective study of disease incidence in African pygmy hedgehogs (*Atelerix albiventris*). *J Vet Med Sci*. 2018;80(10):1504-10.
- Pei-Chi H, Jane-Fang Y, Lih-Chiann W. A Retrospective Study of the Medical Status on 63 African Hedgehogs (*Atelerix albiventris*) at the Taipei Zoo from 2003 to 2011. *J Exot Pet Med* 2015;24(1):105-11.
- Raymond JT, Garner MM. Spontaneous tumours in captive African hedgehogs (*Atelerix albiventris*): a retrospective study. *J Comp Pathol*. 2001;124(2-3):128-33.
- Raymond JT, White MR. Necropsy and histopathologic findings in 14 African hedgehogs (*Atelerix albiventris*): a retrospective study. *J Zoo Wildl Med*. 1999;30(2):273-7.
- Silva GF, Rêma A, Teixeira S, Pires MDA, Taulescu M, Amorim I. Pathological findings in African pygmy hedgehogs admitted into a Portuguese rehabilitation center. *Animals*. 2022;12(11):1361.
- Son NV, Chambers JK, Dung LT, Kishimoto TE, Nishimura M, Kita C, Takada Y, Miwa Y, Nakayama H, Uchida K. Histological and immunohistochemical features of normal histiocytes and Langerhans cells, and histiocytic sarcomas in four-toed hedgehogs (*Atelerix albiventris*). *J Comp Pathol*. 2020;178:32-40.
- Stünzi H, Head KW, Nielsen SW. Tumours of the lung. *Bull World Health Organ*. 1974;50(1-2):9-19.
- Takahashi E, Nakamura S. Histiocytic sarcoma: an updated literature review based on the 2008 WHO classification. *J Clin Exp Hematop*. 2013;53(1):1-8.
- Valli VE, Kiupel M, Bienzle D. Histiocytic proliferative diseases. In: Maxie MG, editor. *Jubb, Kennedy & Palmer's Pathology of domestic animals*. 6th ed. St. Louis: Elsevier; 2016. p. 243-55.
- Wilson DW. Tumors of the respiratory tract. In: Meuten DJ, editor. *Tumors in Domestic Animals*. 5th ed. Ames: Wiley Blackwell; 2017. p. 467-98.