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Original Article
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Clinical, pathological and immunohistochemical characterization of spontaneous neoplasms in pet rodents in Northeastern Brazil[1]

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ABSTRACT.- Pereira R.M.F., Lima T.S., Oliveira R.L., Fonseca S.M.C., Wicpolt N.S., Farias R.C., Lucena R.B., Pavarini S.P., Leal de Araújo J. & Mendonça F.S. 2024. **Clinical, pathological and immunohistochemical characterization of spontaneous neoplasms in pet rodents in Northeastern Brazil.** *Pesquisa Veterinária Brasileira 44:e07410, 2024.* Laboratório de Diagnóstico Animal, Universidade Federal Rural de Pernambuco, Recife, Pernambuco, Brazil. E-mail: fabio.mendonca@ufrpe.br

In the last decade, there has been a significant increase in the demand for small rodents such as hamsters, guinea pigs, rats, and mice to be kept as pets. Consequently, the veterinary care provided to these animals has also increased. The aim of this study was to describe gross, histopathological and immunohistochemical findings of 26 spontaneous neoplasms diagnosed in 25 pet rodents in Northeastern Brazil. A retrospective study was carried out from 2014 to 2022 in two veterinary diagnostic laboratories to identify cases of tumoriform lesions in these species. Hamsters represented the most frequent species in this study (60%, 15/25), followed by rats (28%, 7/25), guinea pigs (8%, 2/25), and mice (4%, 1/25), with a mean age of 17.63 months. The anatomical regions of the face/head and thoracic region were the most affected. The most affected tissues were the skin/subcutaneous/mucosal (65%, 15/26) and mammary gland (23%, 6/26). Eighteen different types of neoplasms were diagnosed, and T-cell lymphomas and mammary adenocarcinomas were the most diagnosed tumors, each corresponding to 12% (3/26) of the cases. Leiomyosarcoma, myxosarcoma and mammary adenocarcinoma metastases were also noted. Immunohistochemistry was essential for the diagnosis of certain malignant mesenchymal and round-cell neoplasms. Pet rodent neoplasms in Northeastern Brazil are common, especially in hamsters, and immunohistochemistry can be a useful tool for the definitive diagnosis of these tumors.

INDEX TERMS: Guinea pig, hamster, mouse, rat, rodentia, tumors, histopathology, immunohistochemistry.

INTRODUCTION

Rodent species such as guinea pigs (*Cavia porcellus*), Syrian hamsters (*Mesocricetus auratus*), dwarf hamsters (*Phodopus* spp.), Chinese hamsters (*Cricetulus griseus*), rats (*Rattus norvegicus*) and mice (*Mus musculus*), have exponentially increased in popularity as companion animals (Mancinelli & Capello 2016). However, most of the scientific literature on diseases of pet rodents has been indiscriminately extrapolated from the knowledge acquired from laboratory rodents (Brown & Donnelly 2012). The most frequently observed health issues in these animals encompass traumatic injuries, infectious and parasitic diseases, nutritional diseases, aging-related disorders, and neoplasms (Brown & Donnelly 2012).

Data regarding the incidence of spontaneous neoplasms in pet rodents are still conflicting. Some researchers report a higher incidence of spontaneous neoplasms in rats and mice. In contrast, in hamsters, this occurrence is reported to be below 3.7%, accompanied by a wider spectrum of tumor

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types (Greenacre 2004). On the other hand, some authors indicate that the incidence of spontaneous tumors in hamsters around two years of age ranges from 50% or more (Harkness & Wagner 1995). In guinea pigs, spontaneous neoplasms are uncommon, and although tumors have been documented as early as six weeks of age, they become more frequent after three years of age (Suarez-Bonnet et al. 2010).

Serial studies of spontaneous neoplasms in pet rodents are still scarce, and most of them focus on hamster species (Kondo et al. 2008b, Kondo et al. 2009, Yoshimura et al. 2015, Wentz et al. 2020, Rother et al. 2021). Other studies focus on mammary tumors of guinea pigs (Suarez-Bonnet et al. 2010) and neoplasms of only rats and mice (Trotte et al. 2008, 2010).

To date, there is only one retrospective study in Brazil on naturally occurring neoplasms of pet rodent species (Wentz et al. 2020). Therefore, the aim of this study was to describe the gross, histopathological, and immunohistochemical features of spontaneous neoplasms of hamsters, rats, guinea pigs, and mice kept as pets in Northeastern Brazil.

MATERIALS AND METHODS

Animal Ethics. This study was conducted following the guidelines proposed by the University Institutional Ethics on Animal Use Committee (CEUA) of the "Universidade Federal da Paraíba" (UFPB), which approved the use of the tissues for teaching and research for patients upon submission for necropsy, protocol number: 9756290419.

All cases of surgical pathology and necropsy of pet rodents submitted to the "Laboratório de Diagnóstico Animal" (Laboratory of Animal Diagnosis – LDA) at the "Universidade Federal Rural de Pernambuco" (UFRPE) and to the "Laboratório de Patologia Veterinária" (Laboratory of Veterinary Pathology – LPV) at the UFPB from 2014 to 2022 were reviewed. For this study, the inclusion criteria consisted of masses or plaques in the tegument or internal organs of rodents kept as companion animals.

Data on affected species, sex, age, origin, affected anatomical site, as well as macroscopic and microscopic findings, were reviewed. After the selection of the cases, histopathological slides were reanalyzed, as well as their photographic records. New histopathological sections were prepared from tissues embedded in paraffin and stained with hematoxylin and eosin (HE) when necessary. Additionally, special stains, such as Alcian blue (AB) at a pH of 2.5, were performed when needed.

Based on histopathological features, tumors were divided into mesenchymal and epithelial neoplasms and these groups were further subdivided based on the specific tissue affected and their anatomical location. For selected cases, immunohistochemistry was performed to confirm the neoplasms' cellular origin. Briefly, immunohistochemistry was performed as follows: 4μM histological sections were deparaffinized in xylene, hydrated in decreasing concentrations of ethanol, and washed in distilled water. They were then subjected to antigenic recovery by heating in a high pH solution (Target Retrieval solution High pH-DM828, K800221-2 EnV FLEX+, High pH Link, Dako) in a pressure cooker (PascalR, Dako). Subsequently, the slides were placed at room temperature for 20 minutes for cooling and washed with deionized water. Blocking of endogenous peroxidase was performed by immersing slides in ready-to-use hydrogen peroxide (EnVisionTM FLEX PEROXIDASE-BLOCKING REAGENT SM801, K800221-2 EnV FLEX+, High pH Link, Dako). After this step, the sections were washed in tris solution (pH 7.4), and then the nonspecific sites were blocked with nonspecific reaction-blocking solution (protein block serum-free – Dako, X0909). Incubation with primary antibody was performed for 18 hours at 4°C. An amplification and detection system (EnVision FLEX/HRP, SM802 (Dako) and diaminobenzidine (DAB) chromogen (EnVision FLEX DAB+CHROMOGEN, DM827, Dako) were used. Slides were counterstained with Harris' hematoxylin. Depending on the histopathological features of each neoplasm, primary antibodies against CD3, CD79, Ki67, Factor VIII, vimentin, desmin, alpha-smooth muscle actin, or Iba-1 were used. Standardized positive controls for each antibody were run in parallel. In negative control sections, primary antibodies were replaced by phosphate-buffered saline (PBS).

RESULTS

General comments

Thirty tumoriform lesions were diagnosed in 29 pet rodents. Most of which were spontaneous neoplasms (26/30). A smaller number of non-neoplastic tumors (4/30) were identified in rats (chronic pododermatitis, mammary gland ectasia and hyperplasia) and a Syrian hamster (dental abscess).

A total of 26 spontaneous neoplasms were diagnosed in 25 pet rodents. The neoplasms analyzed by surgical biopsy (77%, 20/26) were more frequent than those obtained by necropsy (23%, 6/26). The following results were calculated based on the total number of rodents.

Hamsters were the main affected species (60%, 15/25), followed by rats (28%, 7/25), guinea pigs (8%, 2/25) and mice (4%, 1/25). Considering the hamster species, Russian dwarf hamsters were the most common (28%, 7/25), followed by Syrian hamsters (24%, 6/25) and Chinese hamsters (8%, 2/25). Only one rodent, a Russian dwarf hamster, had two different types of neoplasms (Case 8).

In general, regarding the sex of rodents, the distribution between males (52%, 13/25) and females (48%, 12/25) was similar. As for the age group, 60% (15/25) of the rodents aged between 12 and 24 months, while patients aged up to 11 months and over 24 months corresponded to 8% (2/25) each. Age was not informed in 24% (6/25) of the cases. Out of the cases where age was informed, the average age was 17.63 months, ranging from three to 36 months. Individually, the average age of the hamsters was 15.46 months, ranging from three to 36 months, while the rats had an average of 24.5 months, ranging from 14 to 36 months. Guinea pigs and mice did not have enough data to perform these calculations.

The data were calculated based on the number of neoplasms regarding the anatomical sites and tissues affected. The affected anatomical sites are represented in Figure 1. The head/face and thoracic/costal regions were the most affected, each corresponding to 27% (7/26) of the cases, followed by the abdominal/inguinal regions (15%, 4/26 each). The other sites involved included the cervical region (8%, 2/26), flank (4%, 1/26), limbs (4%, 1/26), and internal organs (4%, 1/26). In 8% (2/26) of the cases, the lesions involved multifocal areas of the skin, and in one case, there was no information on where the mass was observed exactly. Regarding the affected tissues, the skin, subcutaneous tissue, or mucosal neoplasms represented 65% of the cases (17/26), while the mammary gland was the second most frequently affected tissue in this study (23%, 6/26). Other tissues included the uterus, cheek pouch, and salivary gland, all with the same frequency (4%, 1/26).

Mesenchymal tumors were more frequent (65%, 17/26) than epithelial tumors (35%, 9/26). Malignant mesenchymal neoplasms (76%, 13/17) were more frequent than their benign counterpart (24%, 4/17). Likewise, the number of malignant epithelial neoplasms was higher than the benign epithelial ones, each corresponding to five and four cases, respectively. The frequency of all diagnosed neoplasms is summarized in Table 1.

In a total of 15 hamsters, 16 neoplasms were diagnosed. Cutaneous T-cell lymphomas, histiocytic sarcomas, myxomas and squamous cell carcinomas (SCC) corresponded to 13% (2/16) of the cases. Other neoplasms included leiomyosarcoma, hemangiosarcoma, myxosarcoma, atypical fibrosarcoma, fibrosarcoma, scent gland adenoma, salivary gland adenoma,

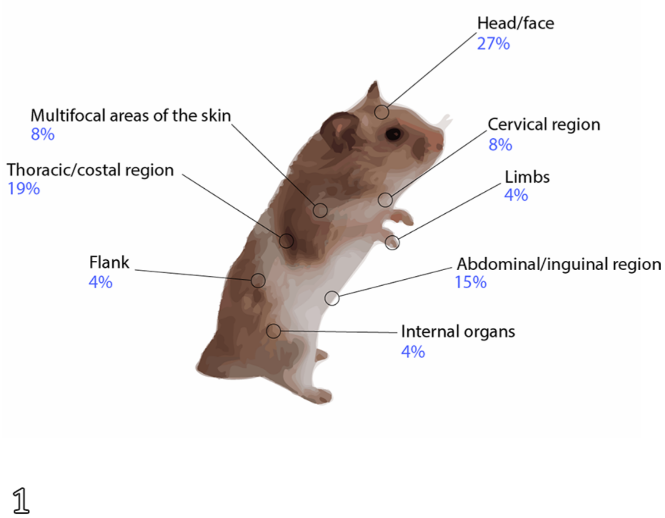

Fig.1. Most affected areas by neoplasms in pet rodents from Northeastern Brazil.

Table 1. Number of cases and frequency of neoplasms diagnosed in pet rodents

Histopathological diagnosis	N	%
Mammary adenocarcinoma	3	12%
T-cell lymphoma	3	12%
Squamous cell carcinoma	2	8%
Myxoma	2	8%
Histiocytic sarcoma	2	8%
Mammary fibroadenoma	2	8%
Mammary fibrosarcoma	1	4%
Atipic fibrosarcoma	1	4%
Fibrosarcoma	1	4%
Anaplastic sarcoma	1	4%
Scent gland adenoma	1	4%
Salivary gland adenoma	1	4%
Fibrolipoma	1	4%
Hemangiosarcoma	1	4%
Leiomyosarcoma	1	4%
Liposarcoma	1	4%
Myxosarcoma	1	4%
Perivascular wall tumor	1	4%
TOTAL	26	100%

and mammary adenocarcinoma, each corresponding to 6% (1/16) of the cases.

In rats, two cases of mammary fibroadenomas were diagnosed. The remaining neoplasms included mammary fibrosarcoma, liposarcoma, fibrolipoma, perivascular wall tumor and one mammary adenocarcinoma, each corresponding to one case. In guinea pigs, an eyelid T-cell lymphoma and an anaplastic sarcoma were diagnosed. In the mouse, a mammary adenocarcinoma was the only neoplasm diagnosed.

Metastasis (12%, 3/26) were more common in hamsters, including a uterine leiomyosarcoma with spread to the spleen and a primary cheek pouch myxosarcoma with metastasis to the abdominal region. In the mouse, there was a metastasis of a mammary adenocarcinoma to the lung.

In 31% (8/26) of the cases, the diagnosis was confirmed by immunohistochemistry. In all these cases, the tumors were malignant mesenchymal or round cell neoplasms, such as leiomyosarcoma, fibrosarcoma, T-cell lymphoma, histiocytic sarcoma, anaplastic sarcoma and a myxosarcoma.

Results are summarized in Table 2. Briefly, the main groups of neoplasms are described below.

Cutaneous or mucosal neoplasms

Cutaneous or mucosal neoplasms were the most common type of tumors in this study. Lymphomas were diagnosed in two Syrian hamsters and one guinea pig, corresponding to 12% (3/26). In a guinea pig, a T-cell lymphoma affected the palpebral conjunctiva (Case 16) and presented clinically as a third eyelid swelling (Fig.2), while in hamster, T-cell lymphomas were restricted to the skin (Fig.3). Microscopically, the neoplasm was characterized by a dense population of round cells arranged in a mantle and supported by moderate fibrovascular stroma (Fig.4). The cases were submitted to immunohistochemistry. All showed positive immunolabeling for CD3 (Fig.5).

Histiocytic sarcomas corresponded to 8% (2/26) of the cases. They were diagnosed by surgical biopsy in two young Syrian hamsters (Cases 5 and 10), all restricted to the skin and subcutaneous tissue. In Case 5, the tumor was located in the periauricular region (Fig.6). Microscopically, the tumors were characterized by a dense population of neoplastic cells with imprecise borders, and scarce to moderate eosinophilic cytoplasm (Fig.7). Immunohistochemical analysis revealed that the neoplastic cells had positive membranous cytoplasmic expression of anti-Iba-1 antibody (Fig.7). An anaplastic sarcoma was diagnosed in a guinea pig with a cutaneous cervical mass and presented histopathological characteristics similar to those observed in the histiocytic sarcomas, however, the neoplasm only exhibited positive immunolabeling for vimentin.

Myxoid neoplasms corresponded to 12% (3/26) of the cases, and they all were diagnosed in adult hamsters. These neoplasms included a cheek pouch myxosarcoma with metastasis to the abdomen (Case 6, Fig.8) and two myxomas in the subcutaneous tissue (Case 7 and 8A), representing 4% and 8% of the cases, respectively. Case 7 refers to a myxoma in the costal region of a Syrian hamster that was referred for biopsy (Fig.9). Microscopically, myxomas appeared as expansive masses of low to moderate cellularity composed of fusiform to stellate cells with imprecise limits and immersed in an abundant basophilic myxoid matrix (Fig.10). The myxosarcoma exhibited the same microscopic characteristics as the myxoma and additionally showed large nuclei with up to three evident nucleoli and up to two mitotic figures per a field area of 0.237mm^2. Positive immunolabeling for vimentin in association with positive AB (Fig.11) confirmed the diagnosis of myxosarcoma. A hemangiosarcoma (Case 8B) was diagnosed in the same hamster that presented a myxoma. In this case, a firm, non-adherent mass was observed, measuring 2cm in diameter in the cervical region, which impaired the animal's balance when walking. Microscopically, the neoplasm was densely cellular, with fusiform cells of imprecise boundaries supported by a fibrovascular stroma. The cells were arranged in dense bundles, sometimes forming trabeculae that mimicked vascular spaces.

Squamous cell carcinomas corresponded to 8% (2/26) of the cases, and they were all located in the face/head region of Russian dwarf hamsters, being restricted to the skin and subcutaneous tissue. In Case 19, obtained by necropsy, the animal presented an ulcerated neoformation on the face with

Table 2. Case, species, age, location of the lesion and diagnosis of neoplastic and non-neoplastic tumors in rodents

Case	Species	Sex	Age	Anatomical region	Tissue	Diagnosis	Metastasis
				Mesenchymal neoplasms			
1	Chinese hamster	Female	36 months	Internal organ	Uterus	Leiomyosarcoma	x
2	Chinese hamster	Male	20 months	Forearm	Skin/subcutaneous/mucosa	Fibrosarcoma	
3	Syrian hamster	Male	12 months	Multifocal areas	Skin/subcutaneous/mucosa	Cutaneous T-cell lymphoma	
4	Syrian hamster	Male	-	Multifocal areas	Skin/subcutaneous/mucosa	Cutaneous T-cell lymphoma	
5	Syrian hamster	Female	5 months	Head/face	Skin/subcutaneous/mucosa	Histiocytic sarcoma	
6	Syrian hamster	Male	24 months	Head/face	Skin/subcutaneous/mucosa (Cheek pouch)	Myxosarcoma	x
7	Syrian hamster	Female	24 months	Thoracic/costal	Skin/subcutaneous/mucosa	Myxoma	
8A*	Russian dwarf hamster	Male	12 months	Head/face	Skin/subcutaneous/mucosa	Myxoma	
8B*	Russian dwarf hamster	Male	12 months	Cervical	Skin/subcutaneous/mucosa	Hemangiosarcoma	
9	Russian dwarf hamster	Male	12 months	Abdominal/inguinal	Skin/subcutaneous/mucosa	Atypical fibrosarcoma	
10	Russian dwarf hamster	Female	3 months	Thoracic/costal	Skin/subcutaneous/mucosa	Histiocytic sarcoma	
11	Rat	Female	36 months	Thoracic/costal	Skin/subcutaneous/mucosa	Liposarcoma	
12	Rat	Female	24 months	Thoracic/costal	Skin/subcutaneous/mucosa	Fibrolipoma	
13	Rat	Female	-	Thoracic/costal	Skin/subcutaneous/mucosa	Perivascular wall tumor	
14	Rat	Female	14 months	Thoracic/costal	Mammary gland	Mammary fibrosarcoma	
15	Guinea pig	Female	-	Cervical	Skin/subcutaneous/mucosa	Anaplastic sarcoma	
16	Guinea pig	Male	12 months	Head/face	Skin/subcutaneous/mucosa (Eyelid)	T-cell lymphoma	
				Epithelial neoplasms			
17	Syrian hamster	Male	12 months	Flank	Skin/subcutaneous/mucosa (Scent gland)	Scent gland adenoma	
18	Russian dwarf hamster	Male	16 months	Head/face	Salivary gland	Salivary adenoma	
19	Russian dwarf hamster	Male	12 months	Head/face	Skin/subcutaneous/mucosa	Squamous cell carcinoma	
20	Russian dwarf hamster	Male	-	Head/face	Skin/subcutaneous/mucosa	Squamous cell carcinoma	
21	Russian dwarf hamster	Female	13 months	Abdominal/inguinal	Mammary gland	Mammary adenocarcinoma	
22	Mouse	Female	24 months	Thoracic/costal	Mammary gland	Mammay adenocarcinoma	x
23	Rat	Female	24 months	Abdominal/inguinal	Mammary gland	Mammary fibroadenoma	
24	Rat	Male	-	-	Mammary gland	Mammary fibroadenoma	
25	Rat	Male	-	Abdominal/inguinal	Mammary gland	Mammary adenocarcinoma	

* The animal had two distinct neoplasms.

formation of crusts (Fig.12). Neoplastic keratinocytes were arranged in nests containing eosinophilic concentric lamellae (keratin pearls) at their centers (Fig.13).

One fibrosarcoma (Case 2) and one atypical fibrosarcoma (Case 9) were diagnosed by surgical biopsy in adult hamsters, representing 8% (2/26) of the cases. Tumors were restricted to the skin and subcutaneous tissue. The fibrosarcoma was diagnosed in a Chinese hamster and appeared as a firm, infiltrative nodule on the forearm (Fig.14). Microscopically, the neoplasm was infiltrative, composed of pleomorphic fusiform

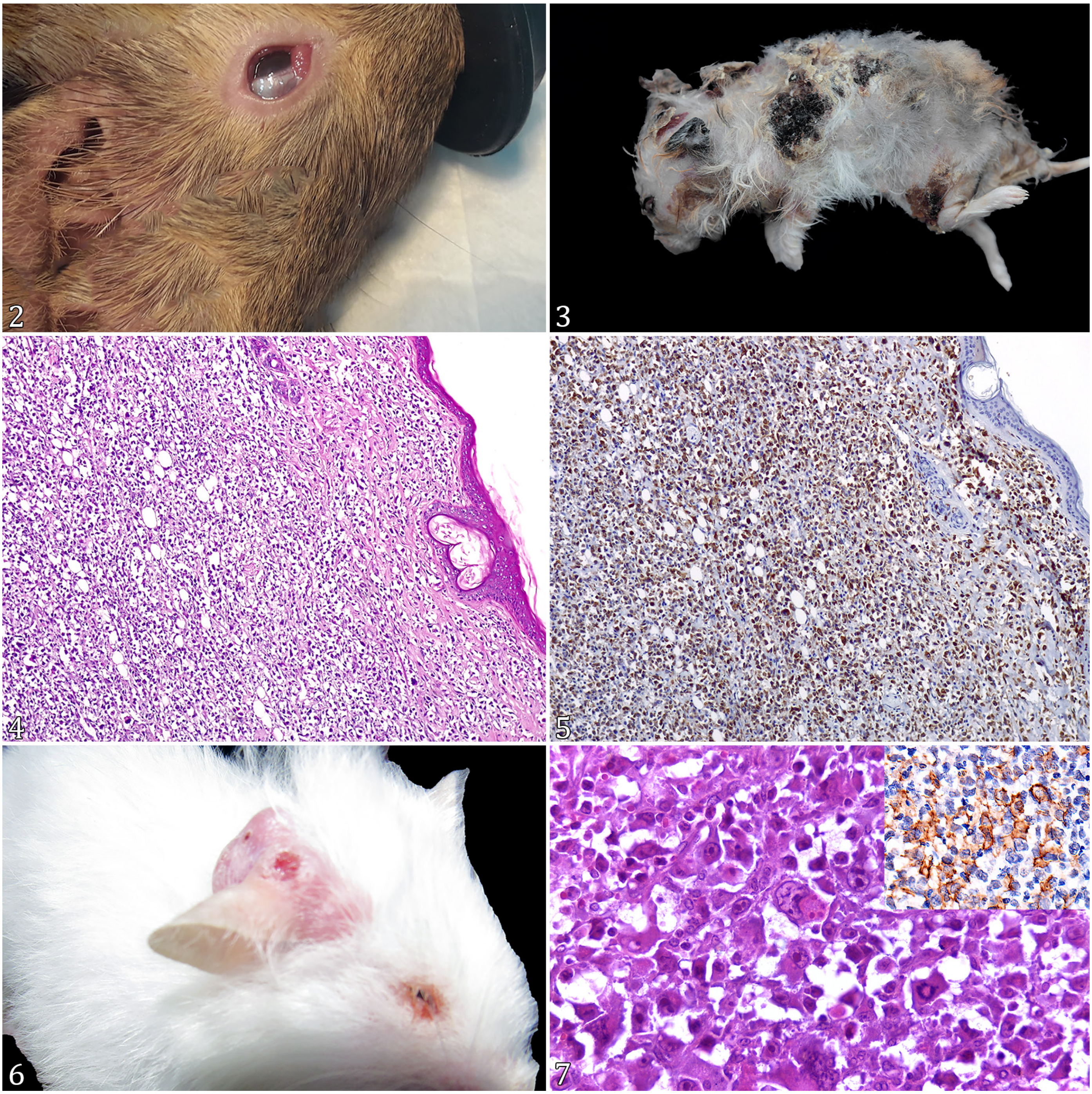

Fig.2-7. Cutaneous and conjunctival neoplasms, rodents. (**2**) Lymphoma, eyelid, guinea pig, Case 16. Rough surface red swelling in the conjunctiva of the third eyelid. (**3**) Cutaneous lymphoma, skin, Syrian hamster, Case 3. Multifocal mildly elevated and crusted lesions with focal skin detachment on the head. (**4**) Cutaneous lymphoma, skin, Syrian hamster, Case 3. Densely cellular, expansive, infiltrative mass extending from the superficial to the deep dermis. HE, obj.10x. (**5**) Cutaneous lymphoma, skin, Syrian hamster, Case 3. Neoplastic cells have positive cytoplasmic immunolabelling for anti-CD3. IHC, obj.10x. (**6**) Histiocytic sarcoma, skin, Syrian hamster, Case 10. Periauricular mass with an irregular and ulcerative surface. (**7**) Histiocytic sarcoma, skin, albino Syrian hamster, Case 10. Highly pleomorphic malignant mesenchymal cells with kidney-shaped nuclei and atypical mitoses. Note the presence of erythrophagocytosis. HE, obj.40x. Inset: Neoplastic cells have cytoplasmic and membranous immunolabelling for Iba-1. IHC, obj.40x.

cells organized in intertwined multidirectional bundles and supported by dense fibrovascular stroma (Fig.15). The neoplasm had positive immunolabelling for vimentin (Fig.15). An atypical fibrosarcoma was diagnosed in a Russian dwarf hamster. The neoplasm appeared as a large subcutaneous nodule in the posterior abdominal region (Fig.16). Microscopically, the tumor was moderately cellular, well-demarcated, multilobulated, and non-encapsulated. Neoplastic cells were large, polygonal to fusiform, and resembled ganglion cells (Fig.17).

Lipomatous neoplasms corresponded to 8% (2/26) of the cases, and they were all diagnosed by surgical biopsy in adult rats. A liposarcoma (Case 11) appeared as an increase

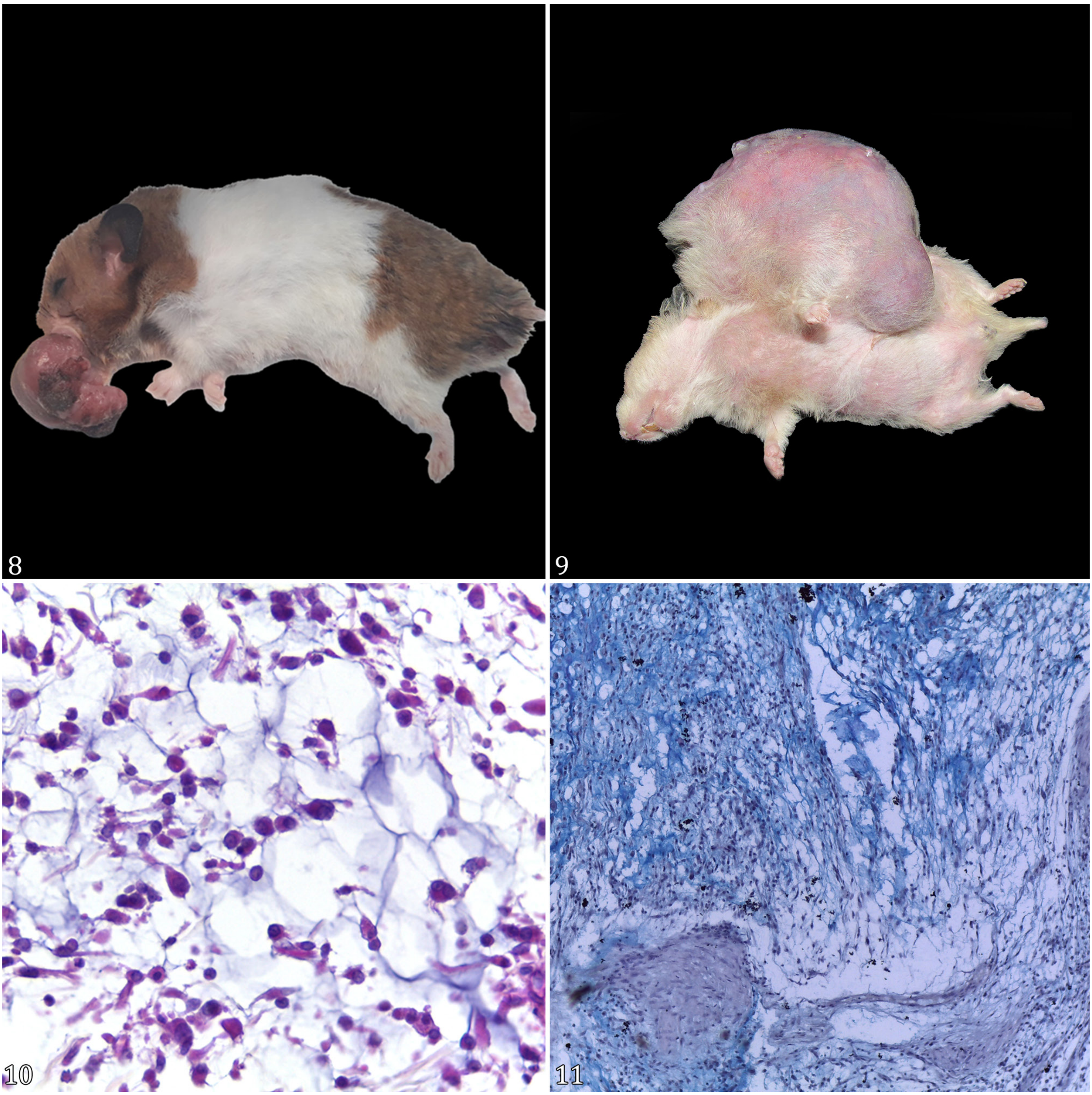

Fig.8-11. Myxomatous neoplasms, rodents. (**8**) Myxosarcoma, cheek pouch, Syrian hamster, Case 6. Multilobulated, red, ulcerated nodule that culminated in distention and reversal of the cheek pouch. (**9**) Myxoma, subcutaneous, Syrian hamster, Case 7. Massive and poorly defined subcutaneous tissue. Mass with irregular contours and covered by intact skin protruding from the costal region. (**10**) Myxosarcoma, costal region, Syrian hamster, Case 6. Fusiform to stellate cells with imprecise limits and immersed in an abundant basophilic myxoid matrix. Note moderate binucleations and anisocytosis to anisokaryosis. HE, obj.40x. (**11**) Myxosarcoma, costal region, Syrian hamster, Case 6. Malignant mesenchymal cells supported by positive alcian blue myxoid matrix. Alcian Blue stain, obj.10x.

in volume in the axillary region. Microscopically, the tumor was composed predominantly of round cells with precise boundaries and cytoplasm containing large vacuoles (Fig.18).

A fibrolipoma (Case 12) appeared as a firm nodule in the costal region. Under microscopy, mature adipocytes were observed amid well-differentiated fibrous connective tissue.

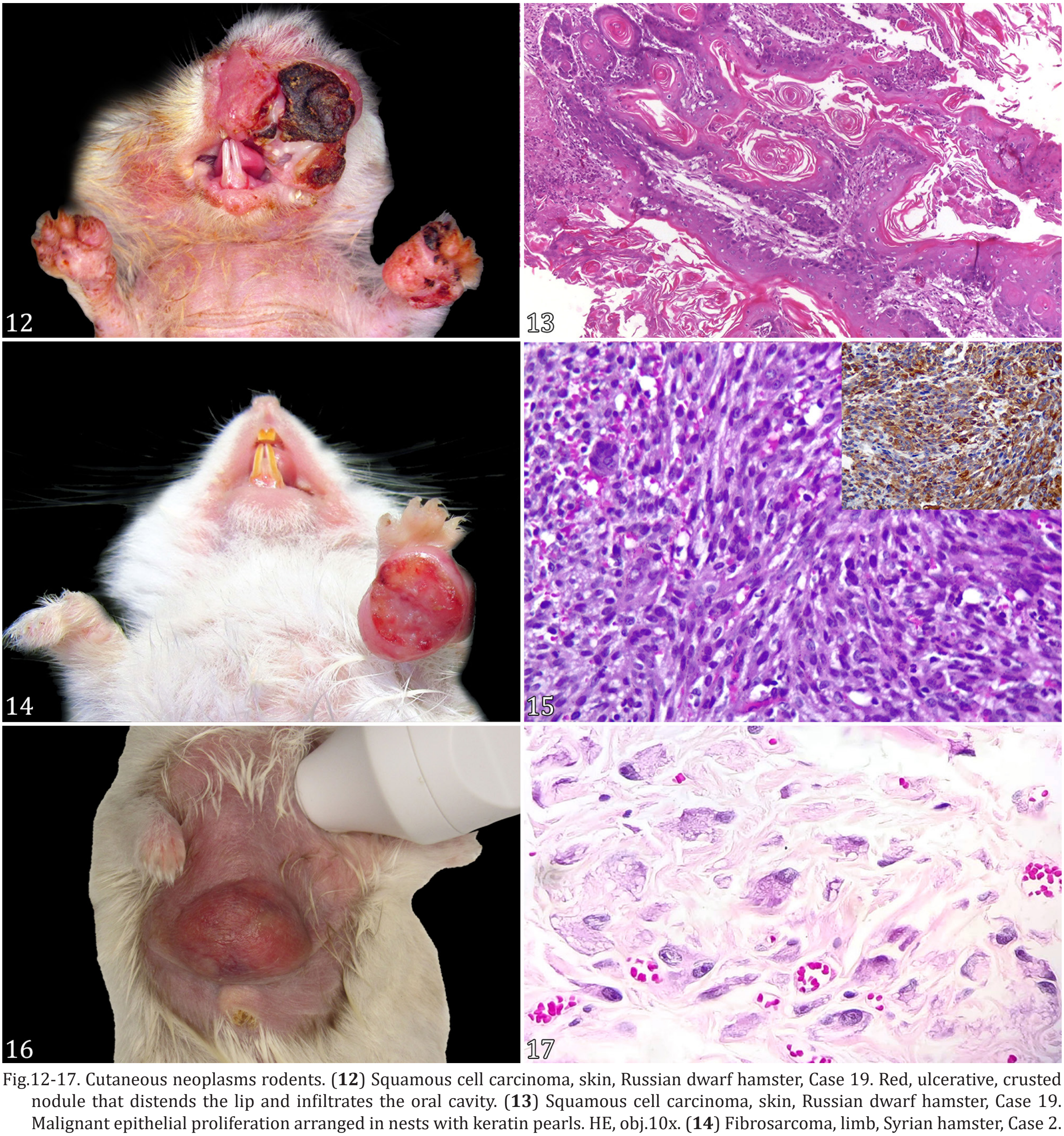

Fig.12-17. Cutaneous neoplasms rodents. (**12**) Squamous cell carcinoma, skin, Russian dwarf hamster, Case 19. Red, ulcerative, crusted nodule that distends the lip and infiltrates the oral cavity. (**13**) Squamous cell carcinoma, skin, Russian dwarf hamster, Case 19. Malignant epithelial proliferation arranged in nests with keratin pearls. HE, obj.10x. (**14**) Fibrosarcoma, limb, Syrian hamster, Case 2. Red, ulcerated nodule in the forearm region. (**15**) Fibrosarcoma, limb, Syrian hamster, Case 2. Pleomorphic spindle cells arranged in bundles and supported by dense fibrovascular stroma. HE, obj.40x. Inset: Note the presence of a multinucleated giant cell and cytoplasmic immunolabelling for vimentin. IHC, obj.40x. (**16**) Atypical fibrosarcoma, skin, Russian dwarf hamster, Case 9. Well-circumscribed nodule covered by alopecic, intact, red skin in the caudal abdominal region. (**17**) Atypical fibrosarcoma, skin, Russian dwarf hamster, Case 9. Polygonal cell proliferation supported by delicate fibrovascular stroma. Note large, amphophilic, fibrillar cytoplasm and eccentric nuclei resembling ganglion cells. HE, obj.40x.

The perivascular wall tumor was diagnosed in a rat by surgical biopsy and was restricted to the skin and subcutaneous tissue (Case 13). The animal presented a rapidly growing mass in the thoracic subcutaneous region. Microscopically, a multilobulated neoformation was observed, composed of a proliferation of spindle cells arranged in spirals around blood capillaries and supported by a collagenous stroma (Fig.19).

The scent gland adenoma was diagnosed in an adult Syrian hamster by surgical biopsy and was restricted to the skin and subcutaneous tissue (Case 17). The neoplasm appeared as a discrete firm black protuberance in the flank region (Fig.20). Microscopically, a non-encapsulated mass with large irregular lobes that expanded into the dermis was observed (Fig.21).

Mammary neoplasms

Mammary neoplasms were the second most diagnosed neoplastic type in this study (23%, 6/26), predominantly those of epithelial origin, such as three cases of mammary adenocarcinoma (12%, 3/26 – Cases 21, 22 and 25) and two cases of mammary fibroadenoma (8%, 2/26 – Cases 23 and 24). A mammary fibrosarcoma (Case 14) was the only mesenchymal origin case, corresponding to 4% of the cases. In Case 21, obtained from a surgical biopsy, the hamster exhibited a nodule in the inguinal region (Fig.22) that drained translucent fluid. Microscopically, the neoplasm was composed of epithelial cells organized in tubular structures of up to two cell layers, surrounded by myoepithelial cells. Occasionally, apocrine secretion was observed within the glandular structures. Case 22 was a mouse referred to *post mortem* examination that presented a solid mammary adenocarcinoma. Microscopically, the epithelial cells were organized in a solid arrangement and supported by a moderate fibrovascular stroma. There were multifocal areas of necrosis, hemorrhage, and neoplastic emboli within the blood and lymphatic vessels. Up to one mitotic figure per field area of $0.237mm^2$ was observed. The same cellular pattern of the mammary tumor was seen in another mass found in the lungs (Fig.23). Mammary fibroadenomas were characterized by proliferation and ectasia of the glandular

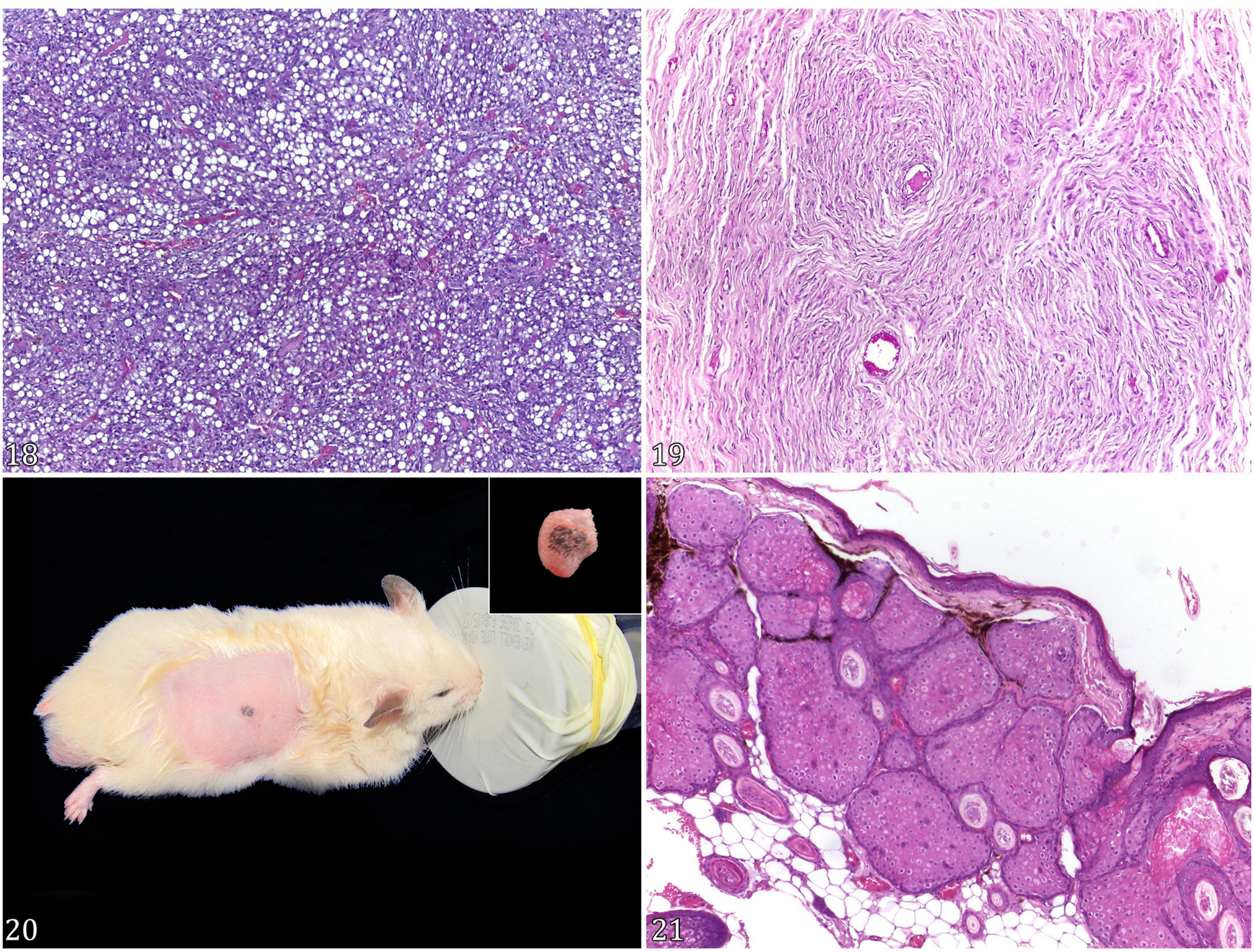

Fig.18-21. Cutaneous neoplasms, rodents. (**18**) Liposarcoma, subcutaneous, rat, Case 11. Proliferation of malignant adipocytes with intensely vacuolated cytoplasm. HE, obj.10x. (**19**) Perivascular wall tumor, subcutaneous, rat, Case 13. Note benign spindle cells organized in whorls that surround the blood capillaries. HE, obj.10x. (**20**) Adenoma of the odor gland, Syrian hamster, Case 17. Inset: Increase in volume with irregular contours in the flank region with better evidence. (**21**) Odor gland adenoma, Syrian hamster, Case 17. Multibolulate mass consisting of benign mature sebocytes. Note lakes of hyaline droplets consistent with sebum secretion. HE, obj.10x.

epithelium, surrounded by intense fibrovascular tissue. Inside the glandular structures, there was apocrine secretion.

Other neoplasms

Leiomyosarcoma was identified in an adult Chinese hamster, referred to as necropsy (Case 1). Masses were observed in the cervix and spleen. Microscopically, a densely cellular neoformation of fusiform cells was observed in the uterine cervix, arranged in multidirectional bundles and interspersed by intense fibrovascular stroma (Fig.24). Both the uterus and the spleen were submitted to immunohistochemistry that revealed positive expression for vimentin (Fig.25) and smooth muscle actin.

Submandibular salivary gland adenoma was diagnosed in an adult Russian dwarf hamster by surgical biopsy and was restricted to the skin and subcutaneous tissue (Case 18). A non-encapsulated, well-delimited mass consisting of cubic epithelial cells with well-defined boundaries and moderate amphophilic cytoplasm with centralized nuclei was observed on microscopy.

DISCUSSION AND CONCLUSION

In this study, hamsters, particularly Russian dwarf hamsters, were the species most affected by neoplastic diseases, aligning with findings from other studies where dwarf hamsters (*Phodopus* spp.) were similarly impacted. Our results also align with other studies where cutaneous neoplasms were the most diagnosed (Kondo et al. 2008b, Wentz et al. 2020, Rother et al. 2021). In a recent study (Dobromylskyj et al. 2023), trichofolliculoma was the most frequently diagnosed neoplasm in guinea pigs. In the current study, neoplasms in

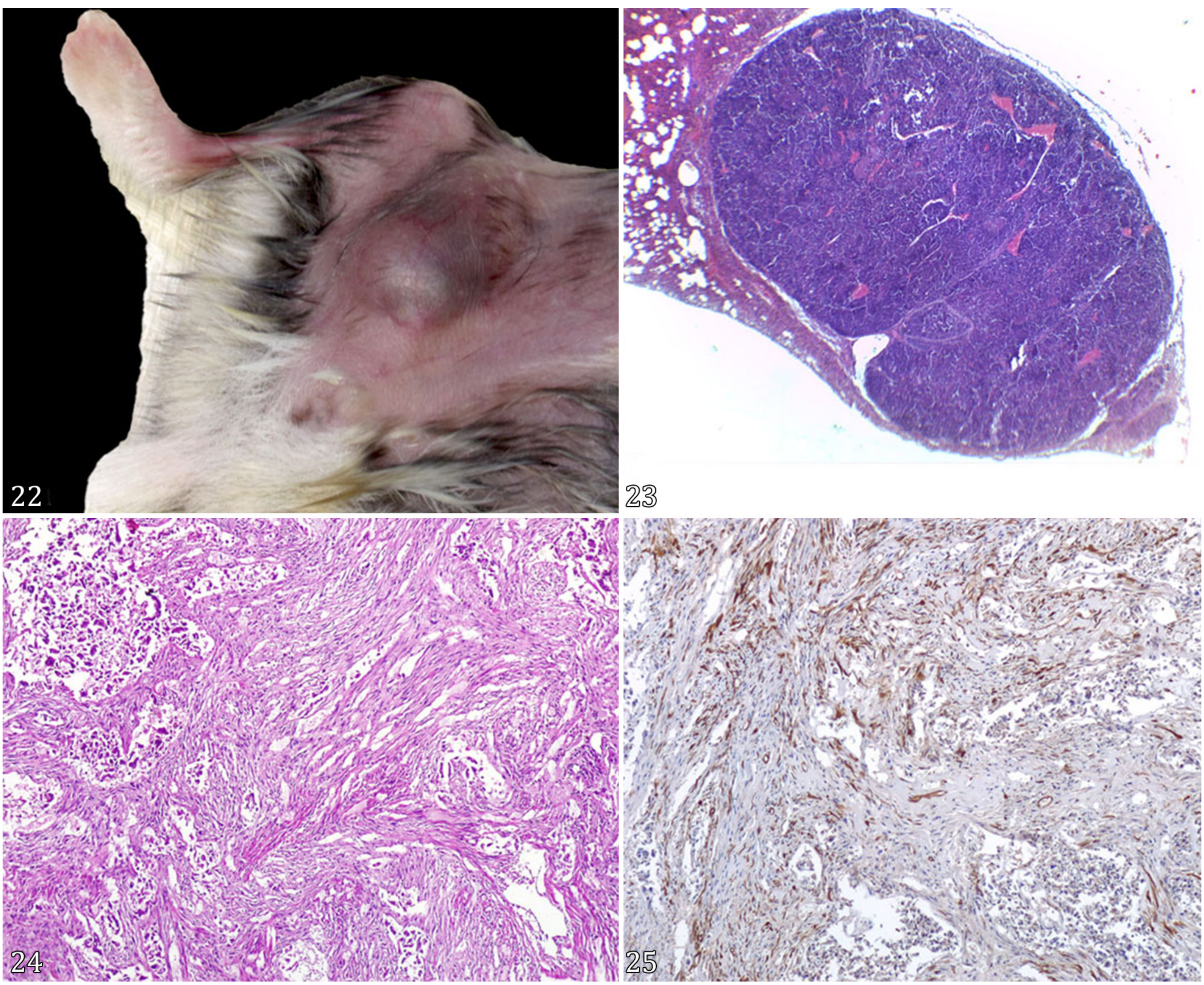

Fig.22-25. Mammary and uterine neoplasms. (**22**) Mammary adenocarcinoma, inguinal region, Russian dwarf hamster, Case 21. Note a purplish nodule covered by skin in the inguinal region. (**23**) Lung metastasis of mammary adenocarcinoma, mouse, Case 22. Note replacement of the lung parenchyma by a densely cellular multilobulated mass with rare acinar formation. HE, obj.4x. (**24**) Leiomyosarcoma, uterus, Chinese hamster, Case 1. Observe the neoplastic leiomyocytes arranged in multidirectional bundles. HE, obj.20x. (**25**) Leiomyosarcoma, uterus, Chinese hamster, Case 1. Positive immunolabelling for smooth muscle actin. IHC, obj.20x.

the skin, subcutaneous tissue or mucosa were predominant and corresponded to 65% of the cases. This trend was also observed in previous rodent studies, where integumentary neoplasms accounted for 60% (Wentz et al. 2020) and 71% (Rother et al. 2021) of the cases. Most of the diseases diagnosed in pet rodents are located in the skin, possibly because it is the most visible portion of the body (Teixeira 2014). Thus, cutaneous neoplasms are more frequently submitted to surgical removal and samples are more likely to be sent to a laboratory (Rother et al. 2021).

Data on the incidence of neoplasms in hamsters have been conflicting (Harkness & Wagner 1995, Greenacre 2004). Although our study showed a higher frequency of neoplasms in hamsters than in other rodent species, this does not necessarily indicate that hamsters are more prone to developing neoplastic diseases. The higher number of samples obtained from hamsters can be attributed to their popularity as pet rodents, leading to more frequent diagnoses and sample submissions (Rother et al. 2021). Regarding Syrian hamsters, some authors state that adrenal gland neoplasms are more common in these species, with a predominance of adenomas over carcinomas (Greenacre 2004, McInnes et al. 2013). However, in our study, these tumors were not observed in any hamster species.

Neoplasms are the main causes of mortality in elderly rodents, while in young rodents less than one-year-old, the causes are usually related to infectious diseases or gastrointestinal problems (Brown & Donnelly 2012). Based on the classification criteria established by Reavill & Imai (2020), where hamsters older than 12 months, rats older than 17 months, mice older than 15 months and guinea pigs older than 36 months are considered geriatric, we identified that more than half of the cases studied were from elderly rodents and only two animals were young. The average age of the hamsters was similar to that of another study with these species, with an average of 19.8 months ranging from five to 36 months (Kondo et al. 2008b).

Lymphoma is one of the most common neoplasms in hamsters (Brown & Donnelly 2012, Hocker et al. 2017, Agueda-Pinto et al. 2019, Wentz et al. 2020), especially in Syrian hamsters (Kamino et al. 2001), as observed in the current study. The cutaneous form of the tumor in hamsters is mainly manifested by multifocal areas of alopecia, desquamation and formation of crusts on the skin (Orr 2011). These characteristics were seen in the hamsters of this study. This clinical manifestation was indicated in some studies as the dominant form (Harvey et al. 1992, Kondo et al. 2008b). However, some authors observed greater involvement of internal organs (Santos et al. 2002, McInnes et al. 2013, Wentz et al. 2020). Immunohistochemistry is essential to determine the cellular origin of lymphomas. In Syrian hamsters with skin lesions similar to the present study, neoplastic cells were strongly positive for anti-CD3, corroborating our results (Harvey et al. 1992). In splenic tumors in hamsters, T-cell and B-cell lymphomas have been identified (Tuan et al. 2018). T-cell lymphomas have also been reported in guinea pigs (Martorell et al. 2011) and squirrels (Honnold et al. 2007). In addition to cutaneous lymphomas, a T-cell lymphoma was also identified in the palpebral conjunctiva of a guinea pig, similar to that observed in another study on the same species (Allgoewer et al. 1999). Conjunctival lymphomas are more frequently described in humans and usually of B-cell lineage (Tanenbaum et al. 2019). Interestingly, in a study on conjunctival lymphomas of dogs and cats (McCowan et al. 2014), all dogs presented T-cell lymphomas, while all cats had B-cell lymphomas. On the other hand, some studies show a variable occurrence of T-cell and B-cell conjunctival lymphomas in these species (Olbertz et al. 2013, Ota-Kuroki et al. 2014, Wiggans et al. 2014).

Histiocytic sarcomas are common in dogs and less frequent in cats (Koizumi & Kondo 2019). However, reports of this neoplasm in hamsters are limited, including cases in Armenian and Siberian hamsters, males aged 14 and 21 months, respectively (Coble et al. 2015, Cheleuitte-Nieves et al. 2021). In a study of splenic neoplasms in dwarf hamsters (*Phodopus* spp.), this tumor was the most observed, corresponding to 33.3% (5/15) of the cases, occurring mostly in females, and with a mean age of 16.6 months (Tuan et al. 2018). In our study, histiocytic sarcomas were diagnosed in a Syrian hamster and a Russian dwarf hamster, and unlike the cases mentioned above, the animals were young, aged between three and five months, and the neoplasms were all located in the skin. Similar to the studies mentioned above, in our study, histiocytic sarcoma was more common in females (Cheleuitte-Nieves et al. 2021). It was not possible to identify if there was involvement of internal organs, as reported in Siberian hamsters and dwarf hamsters, as the samples were from surgical biopsy. The histopathological findings in Case 8 were similar to those observed in a capybara, where numerous multinucleated giant cells were observed, in addition to cells with abundant and intense eosinophilic cytoplasm (Srivoraku et al. 2017). In our study, neoplastic cells were positive for Iba-1, similar to what has been described in an Armenian hamster and a sugar glider (Cheleuitte-Nieves et al. 2021, Son et al. 2021). Additionally, neoplastic cells were also positive for vimentin, which has also been described in a capybara (Srivoraku et al. 2017). Interestingly, in our case of an anaplastic sarcoma in a guinea pig, the multinucleated giant cells showed weak or absent Iba-1 immunolabelling, similar to what has been described in another study with histiocytic sarcoma in a sugar glider (Son et al. 2021). It is believed that the expression of these molecules decreases during the multinucleation of neoplastic cells (Son et al. 2021). In poorly differentiated tumors, very anaplastic cells may not express typical antigens (Mauldin & Peters-Kennedy 2016).

Myxoid neoplasms are infrequent in humans and animal species (Takami et al. 2017) but were common in our study. A myxosarcoma in a Syrian hamster exhibited anatomopathological features similar to the myxoma in Case 7 (Cagnini et al. 2011). Both hamsters were of the same species, two years old and exhibiting a large costal mass. In agreement with our results, cheek pouch myxosarcoma has only been reported in Syrian hamsters so far (Friedell et al. 1960, West et al. 2001, Rother et al. 2021); however, unlike Case 6, the metastatic potential of this tumor has not been reported. The histochemical and immunohistochemical results of the myxosarcoma were corroborated by another study with the same species (Cagnini et al. 2011). It is suggested that genetic, environmental, and toxic factors are possible causes of these tumors (Takami et al. 2017); however, in our study, no hamster with myxoid neoplasia presented a history related to these variables.

Most reports of fibrosarcomas in rodents come from laboratory animal experiments (Gilson et al. 1990, Prakash et al. 2001, Smieško et al. 2020). Spontaneous fibrosarcomas in limbs have been reported in pet degus (*Octodon degus*) (Svara et al. 2020), similar to Case 2. In our study, immunohistochemistry was essential to differentiate the tumor from undifferentiated spindle cell sarcomas. Positive immunolabeling for vimentin confirmed its mesenchymal origin. Negative labeling for desmin excluded the possibility of a myogenic tumor, just as the negative labeling for factor VIII excluded the possibility of a poorly differentiated hemangiosarcoma since the tumor exhibited areas similar to vascular channels. Our results were also corroborated by a case report of a fibrosarcoma in the shoulder of a Djungarian hamster (Kondo et al. 2008a).

Atypical fibromas have so far only been diagnosed in dwarf hamsters (Kondo et al. 2011). These neoplasms tend to appear mainly in the abdominal region (50% of the cases), covered by intact, alopecic, red to purple skin. Because they are androgen-dependent, they occur mainly in adult males but have also been reported in females (Baba et al. 2003, Johnson et al. 2014). These tumors are derived from cells similar to ganglion cells in the dermis and subcutaneous tissue of the abdominal region of dwarf hamsters (Kondo et al. 2011). The cells are large and vary from fusiform to polygonal. An important characteristic of this neoplasm is its fibrillar and amphophilic cytoplasm, which resemble neurons (Kondo et al. 2011, Pertl et al. 2019). These gross and microscopic characteristics were present in the current study associated with criteria of malignancy, such as cellular pleomorphism, binucleations and mitoses, similar to those reported in another study (Johnson et al. 2014).

As seen in our study, liposarcomas in rats may occur in the axillary region. Therefore, this tumor must be differentiated from mammary neoplasms, especially mammary fibroadenoma, common in these species (Trotte et al. 2008). Adipocyte neoplasms are infrequent in rodents (Quinton et al. 2013). In a study, out of 2.318 neoplasms in rats, lipoma corresponded to 0.97% and 0.23% of all integumentary tumors for males and females, respectively (Chandra et al. 1992). In guinea pigs, lipomatous neoplasms seem more common (Quinton et al. 2013). In this species, lipomas were more frequent (19%) than liposarcomas (3%) (Reavill & Imai 2020).

SCCs in rodents are more documented in hamsters, mainly affecting the head region and possibly the lips and nasal cavity (Conceição et al. 2018). In Southern Brazil, this neoplasm was responsible for 35% of the cases of tumors in domestic hamsters (Wentz et al. 2020), a higher percentage than the one observed in our study (8%), although similar to what has been observed by other authors in Japan (Kondo et al. 2008b). As in other domestic animals, excessive sunlight exposure might be involved in developing these tumors, as hairless, non-pigmented areas such as the oral cavity, lips, and ears are usually the most affected regions (Wentz et al. 2020).

Although commonly reported in dogs, spontaneous hemangiosarcomas are infrequent in rodents (Machado et al. 2021). Considering the total number of hamsters, hemangiosarcoma was present in only 7% of the cases, similar to other studies with hamsters where the occurrence of this tumor ranged from 1.1% to 6.6% (Kondo et al. 2008b, Tuan et al. 2018, Wentz et al. 2020, Rother et al. 2021). As with these studies, there was no dissemination to other sites, differing from a case report in a Syrian hamster, where there was metastasis to the liver, spleen and lungs (Machado et al. 2021). In rats and mice, the occurrence of this neoplasm is uncommon (Trotte et al. 2008, 2010).

In rodent mammary tumors, apocrine secretions can be observed inside glandular components (Russo & Russo 2000, Urayama et al. 2001, Kondo et al. 2009, Yoshimura et al. 2015), as noted in Cases 21, 23 and 24. It has been suggested that neoplasms with apocrine secretion may originate from sweat glands and that neoplasms in these glands should be differentiated from mammary tumors. It is important to know that rodents do not have sweat glands, except those located on the foot pads; therefore, the location of the neoplasms must be considered as a fundamental factor for the diagnosis (Kondo et al. 2009). Mammary fibroadenoma is the most common mammary neoplasm in rats (Vergneau-Grosset et al. 2016) and was the second most common tumor diagnosed in a study (Trotte et al. 2008), similar to our research. In mice, mammary adenocarcinomas are the most frequent mammary tumors (Trotte et al. 2008, 2010). The solid type has an aggressive biological behavior, and areas of necrosis and lymphatic invasion are commonly reported (Gamba et al. 2017), as occurred in Case 22. In mice, mammary neoplasms can be secondary to infections by mouse mammary tumor virus (MMTV) (Gamba et al. 2017, Lawson et al. 2018, Dutton 2020), a retrovirus of the genus *Lentivirus* (Leal & Fumagalli 2021). However, in the current study, it was not possible to identify whether this case had a viral etiology.

Uterine leiomyosarcoma presented a percentage similar to that observed by other authors, ranging from 1% to 5% (Kondo et al. 2008b, Wentz et al. 2020, Rother et al. 2021). Uterine tumors occur more in geriatric hamsters, and leiomyomas are more frequently reported (Kamino et al. 2001). In a study, this tumor was the most common neoplasm in guinea pigs with a mean age of 48 months and was associated with ovarian cysts (Harkness et al. 2010). It has been suggested that there is a relationship between estrogen-secreting cysts and the development of leiomyomas, as well as in women (Harkness et al. 2010). Our immunohistochemical results are corroborated by a report of a vaginal leiomyosarcoma in a degu (*Octodon degus*), which presented positive immunolabeling for smooth muscle actin and vimentin (Skoric et al. 2010).

The scent gland is a modified sebaceous gland involved in rodents' olfactory communication mechanisms. The diagnosis of odor gland adenoma in the Syrian hamster was based on histopathological criteria similar to those observed in gerbils (Deutschland et al. 2011). In Syrian hamsters, these glands are pigmented, bilateral, and located in the flank region, while in dwarf hamsters and gerbils, the gland is located in the ventral abdominal region (Deutschland et al. 2011, Keeble 2011). In gerbils, odor gland adenoma is the third most common tumor, often inflamed and ulcerated, being the gateway to bacterial infections (Greenacre 2004). So far, there are no reports of this neoplasm in hamsters.

As in domestic animals, reports of salivary gland neoplasms in rodents are rare but are usually carcinomas as reported in chinchillas (Smith et al. 2010), rats (Kobayashi et al. 2010, Li et al. 2013), and in a free-ranging porcupine (Perles et al. 2017). Oral cavity neoplasms in Syrian hamsters are infrequent, and spontaneous salivary tumors are rarely reported (Rainwater et al. 2011).

Perivascular wall tumors (PWTs) represent a group of neoplasms originating from different cells of the perivascular wall and adventitia, except for the endothelium (Avallone et al. 2007). They are classified into hemangiopericytomas, myopericytomas, angioleiomyomas, angiomyofibroblastomas, and angiofibromas according to the component of the affected vessel and immunohistochemistry is vital for tumor identification and classification (Hendrick 2017). In our study, it was not possible to identify the cellular origin, and although these tumors are more common in the limbs, they can also occur in the trunk (Hendrick 2017), as seen in the present case. Hemangiopericytomas have been reported in rodents in rats (Morehead & Barthold 1997, Teixeira et al. 2021) and guinea pigs (Hoch-Ligeti et al. 1980).

We observed in this study that spontaneous neoplasms in pet rodents in Northeastern Brazil are common, especially in hamsters aged around 12 months. The most affected anatomical regions were the head/face and the thoracic region. The most affected tissues were cutaneous/mucosal regions and mammary glands. Lymphomas and mammary adenocarcinomas were the most prevalent neoplasms individually. Immunohistochemistry was essential to confirm the diagnosis of some malignant mesenchymal and round-cell neoplasms, including, for example, T-cell lymphomas in hamsters.

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