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Neoplasms in domestic hamsters in Southern Brazil: epidemiological and pathological aspects of 40 cases[1]

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ABSTRACT.- Wentz M.F., Bianchi M.V., Mello L.S., Pietzsch C.A., Alievi M.M., Driemeier D., Sonne L. & Pavarini S.P. 2020. **Neoplasms in domestic hamsters in Southern Brazil: epidemiological and pathological aspects of 40 cases**. *Pesquisa Veterinária Brasileira 40(12):1029-1038*. Setor de Patologia Veterinária, Faculdade de Veterinária, Universidade Federal do Rio Grande do Sul, Av. Bento Gonçalves 9090, Porto Alegre, RS 91540-000, Brazil. E-mail: saulo.pavarini@ufrgs.br

Although neoplasms are commonly reported in domestic hamsters, retrospective studies approaching spontaneous tumors with data regarding epidemiological findings are scarce. The present study aimed to describe the epidemiological and pathological findings of 40 cases of tumors in domestic hamsters diagnosed in a veterinary pathology laboratory in Southern Brazil from 2002 to 2019. Chinese hamster (*Cricetulus griseus*) was the most commonly affected species (16/40), followed by Djungarian hamster (*Phodopus sungorus,* 11/40) and Syrian hamster (*Mesocricetus auratus,* 4/40). Among the cases, 57.5% were females (23/40), while 42.5% were males (17/40). The affected hamsters' median age was of 14-months old, with an age range of 8- to 36-months old. Twenty-four cases were assessed as anatomopathological samples (biopsies), while 16 were composed of carcasses submitted to postmortem examination, and, therefore, the neoplasm was related to the cause of death. The integumentary system was frequently affected (60%, 24/40), followed by the female reproductive tract (22.5%, 9/40), hematopoietic system (10%, 4/40), digestive tract (5%, 2/40), and endocrine system (2.5%, 1/40). The most frequent neoplasm was squamous cell carcinoma (35%, 14/40), mostly on the lip/nasal region (50%, 7/14). Other tumors included fibrosarcoma (10%, 4/40), lymphoma (10%, 4/40), mammary cystadenoma (10%, 4/40), apocrine sweat gland adenoma (7.5%, 3/40), hemangiosarcoma (5%, 2/40), leiomyosarcoma (5%, 2/40), and granulosa ovarian cell tumor (5%, 2/40). The five remaining cases occurred individually and were composed of hepatoid gland adenoma, solid thyroid carcinoma, cutaneous melanoma, ovarian teratoma, and cutaneous trichoblastoma. Neoplasms were identified as an important cause of death and major reason to perform biopsy in domestic hamsters in Southern Brazil.

INDEX TERMS: Neoplasms, domestic hamsters, Brazil, epidemiology, pathology, spontaneous tumors, oncopathology, rodents, squamous cell carcinoma, lymphoma, fibrosarcoma.

RESUMO.- [**Neoplasias em hamsters domésticos no Sul do Brasil: aspectos epidemiológicos e patológicos de 40 casos.**] Embora neoplasmas em hamsters domésticos sejam comumente relatados, estudos retrospectivos abordando neoplasias espontâneas e os dados epidemiológicos associados são escassos. O presente estudo teve o objetivo de descrever os principais achados epidemiológicos e patológicos de 40 casos de tumores em hamsters domésticos diagnosticados em um laboratório de patologia veterinária do Sul do Brasil de 2002 a 2019. A principal espécie acometida foi o hamster chinês (*Cricetulus griseus*, 16/40), seguido por hamster anão russo siberiano (*Phodopus sungorus*, 11/40) e hamster sírio (*Mesocricetus auratus*, 4/40). As fêmeas corresponderam a 57,5% dos casos (23/40), enquanto os machos representaram 42,5% (17/40). Foram afetados roedores com uma faixa etária de 8 a 36 meses de idade, e uma mediana de 14 meses. Do total de casos, 24 foram exames anatomopatológicos

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(biopsias) e 16 casos foram examinados através de necropsia e, portanto, relacionados com a causa da morte dos animais. O sistema tegumentar foi o mais frequentemente acometido (60%; 24/40), seguido pelo trato reprodutivo (22,5%; 9/40), sistema hematopoietico (10%; 4/40), trato digestório (5%; 2/40) e sistema endócrino (2,5%; 1/40). A neoplasia mais frequentemente diagnosticada foi o carcinoma de células escamosas (35%; 14/40), localizado principalmente em região labionasal (50%; 7/14). Outros tumores incluíram fibrossarcoma (10%; 4/40), linfoma (10%; 4/40), adenoma cístico de glândula mamária (10%; 4/40), adenoma de glândula sudorípara (7,5%; 3/40), hemangiossarcoma (5%; 2/40), leiomiossarcoma (5%; 2/40) e tumor de células da granulosa (5%; 2/40). Os outros cinco casos remanescentes ocorreram individualmente e eram compostos por adenoma de glândula hepatoide, carcinoma sólido de tireoide, melanoma cutâneo, teratoma ovariano e tricoblastoma cutâneo. Neoplasmas foram identificados como importantes causas de morte ou razões para realização de biopsia em hamsters domésticos no Sul do Brasil.

TERMOS DE INDEXAÇÃO: Neoplasias, hamsters domésticos, Brasil, epidemiologia, patologia, tumores espontâneos, oncopatologia, roedores, carcinoma de células escamosas, linfoma, fibrossarcoma.

INTRODUCTION

Hamsters were initially employed as laboratory animals, with significant importance in a medical investigation (Bampi et al. 2014) owing to a supposed low spontaneous tumor incidence and high susceptibility to administered carcinogens (Homburger 1983, Greenacre 2004). However, it became prevalent in the last few decades as a companion or pet animal (Kamino et al. 2001, Kondo et al. 2008). Consequently, veterinary care, such as surgical procedures, has become standard on these rodent patients, as pet owners have increased their demand for quality services (Capello 2011). Among the main species of domestic hamsters worldwide, the Syrian (golden) hamster (*Mesocricetus auratus*) is the most popular (Lennox & Bauck 2012), followed by dwarf hamsters, such as the Djungarian or Russian dwarf hamster (*Phodopus sungorus*) (Jelinek et al. 2013), and the Campbell's Russian dwarf hamster (*Phodopus campbelli*) (Kondo et al. 2008). Moreover, in Brazil, it seems that the Chinese hamster (*Cricetulus griseus*) has become popular in recent years (Conrado et al. 2013, Conceição et al. 2018).

Among the diseases that occur in hamsters, confusing data has been published regarding neoplastic conditions, with studies that report low frequencies of 3.7% (Van Hoosier & Trentin 1979) to highest levels up to 50% in hamsters older than 2-years old (Greenacre 2004). The knowledge regarding its occurrence is mainly related to comprehensive studies aimed at human comparative carcinogenic models (Van Hoosier & Trentin 1979, De Oliveira et al. 2009, Bampi et al. 2014). Other studies have presented these conditions in hamsters as case reports (Santos et al. 2002, Kondo et al. 2006, 2007, 2011, Ghaffari et al. 2009, Martorell et al. 2010, Golbar et al. 2011, Rainwater et al. 2011, Conrado et al. 2013, Jelinek et al. 2013, Johnson et al. 2014, Conceição et al. 2018), disease outbreaks (Coggin et al. 1983), or as retrospective case series in laboratory hamsters (Homburger 1983, Kamino et al. 2001, McInnes et al. 2013), but few have included case series of spontaneous neoplasms in companion animals (Harvey et al. 1992, Kondo et al. 2008). This diagnostic approach is helpful to clinical veterinarians and pathologists in order to obtain a rapid, practical, and precise diagnosis. Therefore, this study aimed to identify and characterize the main epidemiological, gross, and microscopic features of 40 spontaneous neoplasms diagnosed in domestic hamsters through anatomopathological or necropsy exams in Southern Brazil.

MATERIALS AND METHODS

A retrospective study of the anatomopathological and necropsy database in domestic hamsters was conducted to search for records of neoplastic conditions diagnosed from January 2002 to January 2019 at the "Setor de Patologia Veterinária". The materials submitted to the laboratory [fragments of organs in 10% formalin (excisional or incisional biopsies) or refrigerated carcasses] were originated from the "Núcleo de Conservação e Reabilitação de Animais Silvestres" (PRESERVAS) or private veterinary clinics in the metropolitan area of Porto Alegre, Rio Grande do Sul state. Information surrounding the species affected, sex, age, system affected, and anatomical location of the lesion(s) was retrieved from the anatomopathological or necropsy reports and the clinical medical files when available.

After case selection, gross features were evaluated through photographs and previous descriptions present in the reports. Also, paraffin-embedded tissues from these cases were retrieved, cut at 3μm, stained by hematoxylin and eosin (HE), and assessed under light microscopy. These slides were reevaluated, and histological lesions were reclassified. The cases were grouped into nine categories based on the morphological diagnosis: squamous cell carcinoma, lymphoma, fibrosarcoma, mammary cystic adenoma, sweat gland adenoma, hemangiosarcoma, leiomyosarcoma, ovarian granulosa cell tumor, and other neoplasms.

RESULTS

A total of 40 hamsters was diagnosed with a neoplastic condition at the analyzed period. Of these, 24 were assessed as anatomopathological samples (biopsies), while 16 were composed of carcasses submitted to postmortem examination, wherein the neoplasm was regularly identified as the cause of death.

Females accounted for 57.5% of the cases (23/40), while males compiled 42.5% of the total (17/40). Age was provided in 92.5% of cases (37/40), with an age range of 8- to 36-months old and a median age of 14-months old. The species affected were informed in 77.5% of the cases (31/40), of which 16 were Chinese hamsters (*C. griseus,* 51.6%), 11 were Djungarian hamsters (*P. sungorus,* 35.5%), and four were Syrian hamsters (*M. auratus,* 12.9%).

The integumentary system was most frequently affected, accounting for a total of 24 cases (60%), followed by the female reproductive tract (9 cases; 22.5%; ovary, uterus, or mammary glands), hematopoietic system (4 cases, 10%), digestive tract (2 cases, 5%), and endocrine system (1 case, 2.5%).

The absolute frequency and anatomical location according to each neoplastic morphological diagnosis are presented in Table 1. The age, sex, and species affected were also grouped according to each neoplastic morphological diagnosis and are presented accordingly to the absolute frequency of diagnosis in Table 2.

Table 1. Frequency and anatomical location of neoplasms diagnosed in 40 domestic hamsters in Southern Brazil

Neoplasm	N	Frequency	Anatomical location
Squamous cell carcinoma	14	35%	Lip-nasal region: 7/14 (50%) Ear: 3/14 (21.4%) Cheek pouch: 2/14 (14.3%) Skin (submandibular): 1/14 (7.1%) Skin[1]: 1/14 (7.1%)
Lymphoma	4	10%	Multicentric: 3/4 (75%) Lymph node: 1/4 (25%)
Fibrosarcoma	4	10%	Skin (limb): 2/4 (50%) Skin (mammary gland): 1/4 (25%) Skin[1]: 1/4 (25%)
Mammary cystadenoma	4	10%	Mammary gland
Apocrine sweat gland adenoma	3	7.5%	Skin (prepuce): 1/3 (33.3%) Skin (limb): 1/3 (33.3%) Skin (axillary region): 1/3 (33.3%)
Hemangiosarcoma	2	5%	Skin (abdomen): 1/2 (50%) Skin[1]: 1/2 (50%)
Leiomyosarcoma	2	5%	Uterus
Ovarian granulosa cell tumor	2	5%	Ovary
Hepatoid gland adenoma	1	2.5%	Prepuce
Thyroid solid carcinoma	1	2.5%	Thyroid
Cutaneous melanoma	1	2.5%	Skin[1]
Ovarian teratoma	1	2.5%	Ovary
Cutaneous trichoblastoma	1	2.5%	Skin (limb)

N = number of cases; [1] specific anatomical location was not informed.

Table 2. Median age, age range, sex, and species of 40 domestic hamsters according to each neoplasm in Southern Brazil

Neoplasm	N	Median age	Age range	Sex (M:F)	Species affected			
					CH	DH	SH	NA
Squamous cell carcinoma	14	12 m	8 m - 24 m	7:7	7	7	-	-
Lymphoma	4	19.5 m	10 m - 29 m	2:2	2	-	1	1
Fibrosarcoma	4	21 m	12 m - 24 m	1:3	1	1	-	2
Mammary cystadenoma	4	12 m	9 m - 14 m	0:4	2	1	1	1
Apocrine sweat gland adenoma	3	10 m	9 m - 36 m	3:0	-	2	-	1
Hemangiosarcoma	2	20 m	16 m - 24 m	1:1	1	-	-	1
Leiomyosarcoma	2	21 m	18 m - 24 m	0:2	-	-	1	1
Ovarian granulosa cell tumor	2	36 m	36 m - 36 m	0:2	-	-	-	2
Hepatoid gland adenoma	1	24 m	24 m	1:0	1	-	-	-
Thyroid solid carcinoma	1	14 m	14 m	1:0	-	-	1	-
Cutaneous melanoma	1	NA	NA	0:1	-	-	-	1
Ovarian teratoma	1	12 m	12 m	0:1	1	-	-	-
Cutaneous trichoblastoma	1	24 m	24 m	1:0	1	-	-	-

N = number of cases, M = male, F = female, CH = Chinese hamster, DH = Djungarian hamster, SH = Syrian hamster, NA = not available, m = months old.

Squamous cell carcinoma

Squamous cell carcinoma (SCC) was the most common neoplasm identified in this study, accounting for 35% of the cases (14/40), of which six originated from biopsies and eight from necropsies. Of these, five hamsters died promptly after or during surgical resection of the mass. The lip/nasal region was most commonly affected, accounting for 50% of the cases (7/14), of which four had a similar gross pattern with the tumor involving the upper lip and extending into the nasal cavity. These were associated with nasal, maxillary, or mandibular deformations (facial swelling), as invasion and obliteration of the surrounding bones and nasal cavity were frequent, in addition to skin ulceration (Fig.1A-C). The ear was affected in three cases, followed by the cheek (buccal) pouch in two hamsters. Microscopically, masses were composed of neoplastic proliferation of epithelial cells forming fingerlike projections towards the superficial/deep dermis, in addition to multiple nests of neoplastic cells occasionally containing concentrically laminated keratin (keratin pearls). Moreover, a variable degree of the desmoplastic reaction was observed (mild to marked) (Fig.1D).

Lymphoma

Most cases (3/4) were represented by multicentric lymphomas, which were concomitantly identified as the cause of death, while the remaining consisted of a lymph node sample assessed through biopsy. The main organs affected included the lymph nodes (4/4), liver (2/4), spleen (2/4),

kidneys (1/4), small intestine (1/4), mediastinum (1/4), and skin (1/4) (Fig.2A-C). At the necropsy, there were multiple, variable-sized, whitish, soft nodules or masses that on the cut surface were smooth and bright intermixed with red areas. These nodules involved and frequently replaced most of the nodal parenchyma, similarly to other organs affected (spleen, kidneys, and small intestine). Hepatic lymphoma was characterized by focal nodular whitish areas within the parenchyma. Mediastinum or thymic lymphoma was characterized by an extensive whitish mass, which occupied the cranial portion of the thoracic cavity (cranial mediastinum) and displaced/compressed the lungs (atelectasis) in a Chinese hamster. Cutaneous involvement occurred as an extensive alopecic area, interspersed with multiple crateriform nodular lesions at the dorsal thoracic region, cervical region, and head in a Chinese hamster. Microscopically, all the masses were composed by a diffuse neoplastic proliferation of large round cells (larger than two erythrocytes) arranged in mantles. The cells had well-defined cytoplasm, round non-cleaved nuclei, and inconspicuous to single visible nucleoli. A mean mitotic count higher than four mitotic figures per high power field (400x) was noted. Frequently, tingible body macrophages were observed intermingled with the neoplastic lymphocytes, consistent with the 'starry sky' microscopical pattern (Fig.2D). The neoplasms were classified in all cases as high grade diffuse large cell lymphomas.

Fibrosarcoma

Fibrosarcoma was mostly diagnosed through samples assessed as biopsies (3/4), while in one case, it was detected

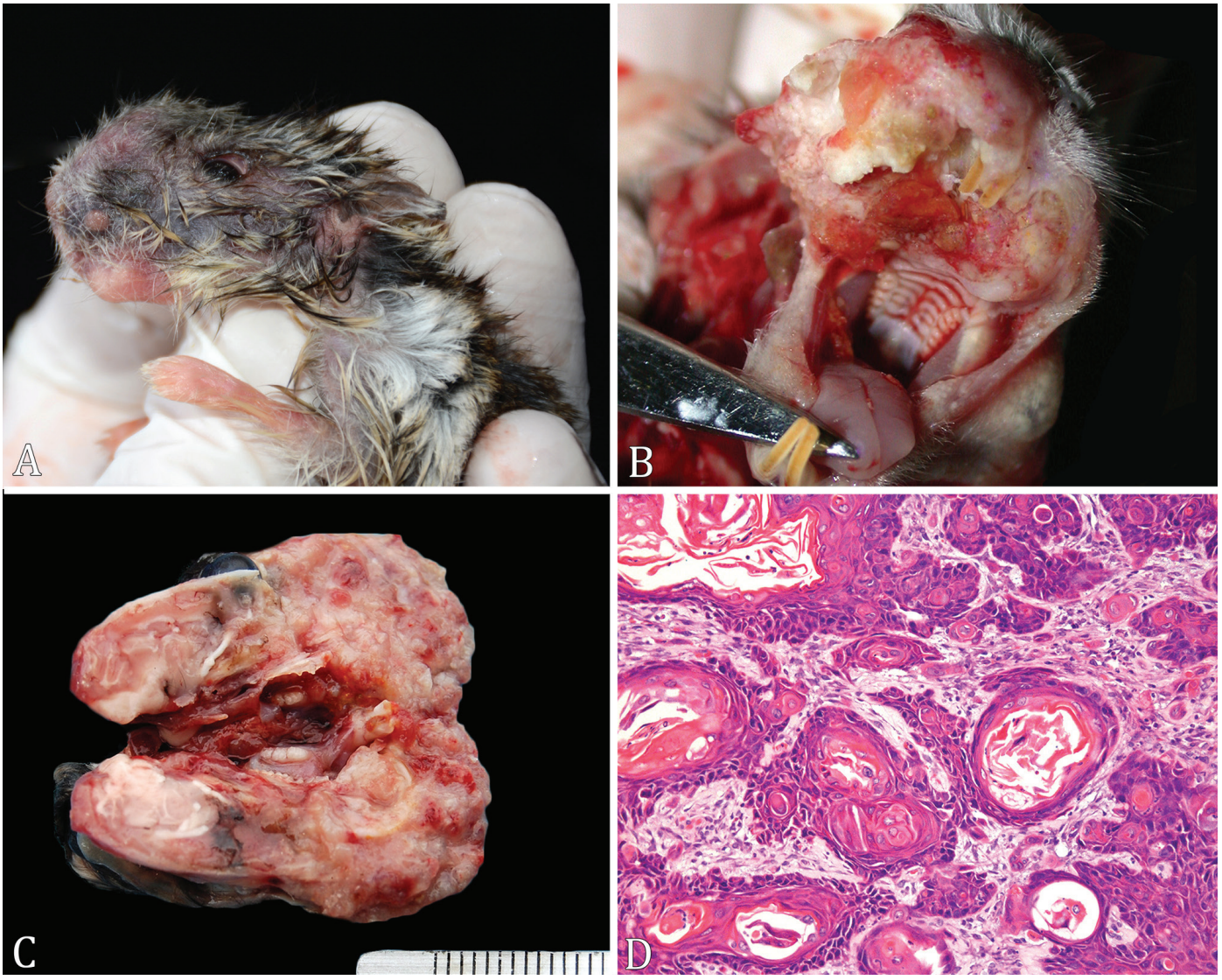

Fig.1. Gross and microscopic findings of squamous cell carcinoma in hamsters in Southern Brazil. (**A**) Djungarian hamster (*Phodopus sungorus*). Facial deformation induced by an increase in volume (mass) at the lip/nasal region. (**B**) Chinese hamster (*Cricetulus griseus*). Whitish mass at the upper lip, which extends into the oral and nasal cavities. (**C**) This mass's cut surface reveals that it completely obliterates the nasal cavity, it is predominantly white, intermixed with red areas, and extends into replacing most of the hard palate. (**D**) Histologically, there is a neoplastic proliferation of epithelial cells arranged in multiple nests with keratin pearls forming at the center. HE, obj.20×.

Fig.2. Gross and microscopic findings of lymphoma in hamsters in Southern Brazil. (**A**) Chinese hamster (*Cricetulus griseus*). The mesenteric lymph node is enlarged and effaced by a predominantly reddish mass intermixed by pinpoint white areas. Besides, the liver presents a focal nodular, white area. (**B**) Chinese hamster (*C. griseus*). A whitish mass occupies the cranial mediastinum at the thoracic cavity, causing pulmonary atelectasis. (**C**) Chinese hamster (*C. griseus*). The dorsum's extensive alopecic area is intermixed with multiple crateriform nodular lesions at the dorsal thoracic region, cervical region, and head. (**D**) Histologically, there is a neoplastic proliferation of large lymphocytes arranged in mantles. Multiple tingible body macrophages are observed intermingled with the neoplastic lymphocytes, giving the lesion a 'starry sky' microscopical pattern. HE, obj.20×.

through necropsy. In all cases, the samples consisted of cutaneous masses, characterized by single, demarcated, and firm to hard nodules, with focal areas of superficial ulceration. Microscopically, the nodules were composed of neoplastic proliferation of spindle cells arranged in bundles in multiple directions. These cells had broad eosinophilic and poorly demarcated cytoplasm, oval nuclei, and evident nucleoli, often multiple per cell. Extensive focal areas of epidermal ulceration associated with neutrophilic infiltrate were frequently noted as well (Fig.3A).

Mammary cystadenoma

Mammary neoplasms were composed solely by benign tumors assessed through biopsy samples, of which mammary cystic adenoma was identified in all cases (4/4). Relatively young females were affected, with a median age of 12-months old. Microscopically, all cases presented multifocal to coalescing areas of adenomatous hyperplasia intermixed with the benign proliferation of epithelial cells, which were frequently arranged in multiple variable size cystic structures (Fig.3B).

Apocrine sweat gland adenoma

Apocrine sweat gland adenoma was diagnosed in three cases, which were assessed through biopsy of skin samples. Grossly, these lesions presented as single and soft nodules that on the cut surface exuded a translucid fluid through cavitations. Histologically, there was a proliferation of columnar epithelial cells arranged in well-differentiated tubular structures,

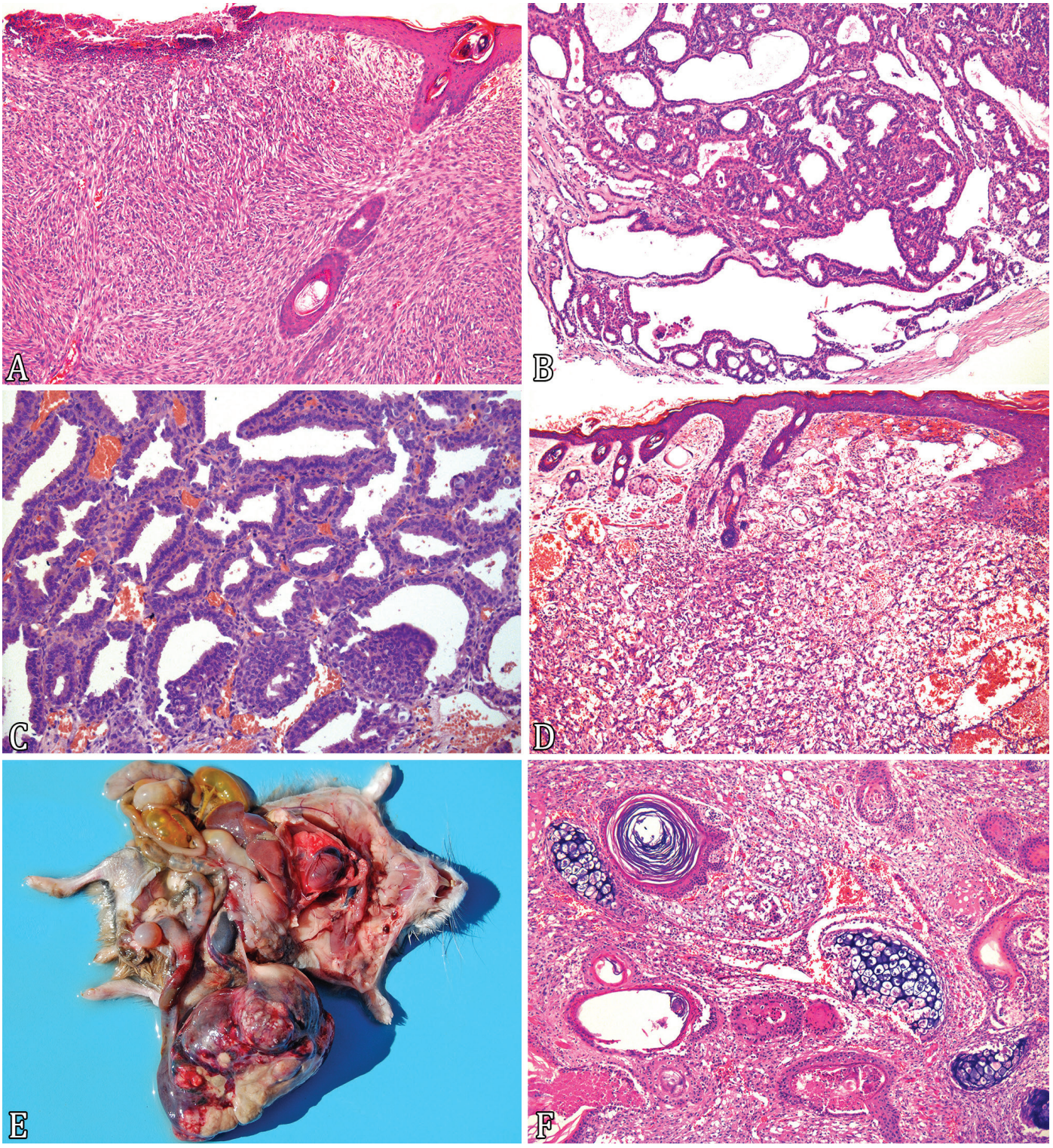

Fig.3. Gross and microscopic findings of other neoplasms diagnosed in hamsters in Southern Brazil. (**A**) Cutaneous fibrosarcoma. The malignant neoplastic proliferation of spindle cells is arranged in bundles in multiple directions at the superficial and deep dermis. A focally extensive area of ulceration at the epidermis is also observed. HE, obj.10×. (**B**) Mammary cystadenoma. The benign neoplastic proliferation of epithelial cells is arranged in multiple cystic areas. HE, obj.10×. (**C**) Sweat gland adenoma. The benign neoplastic proliferation of columnar epithelial cells has abundant granular cytoplasm and is arranged in acinar structures. HE, obj.20×. (**D**) Cutaneous hemangiosarcoma. The neoplastic proliferation of spindle cells at the superficial and deep dermis is arranged in multiple primitive vascular structures filled by erythrocytes. HE, obj.10×. (**E-F**) Ovarian teratoma. Chinese hamster (*Cricetulus griseus*). (**E**) The left ovary is effaced by a whitish-reddish mass, which occupies almost the entire abdominal cavity. (**F**) Microscopically, there is a neoplastic proliferation of cells with multiple germinative origins. The neoplasm forms multifocal random areas of stratified epithelium containing keratin at the center, cartilaginous tissue, muscle fibers, and adipose tissue intermixed with multifocal areas of necrosis. HE, obj.20×.

which contained small amounts of basophilic material within the lumen. Moreover, the cells had an abundant granular cytoplasm, and occasionally apical blebs (characteristic of apocrine glands) were observed (Fig.3C).

Hemangiosarcoma

Hemangiosarcoma was diagnosed through samples assessed as biopsies in two cases, which affected only the skin and were grossly characterized by non-limited red nodular structures. On the cut surface, these exhibited multiple cystic red areas that microscopically consisted of a proliferation of mesenchymal spindle cells arranged in primitive vascular structures filled by variable amounts of erythrocytes. Also, there were extensive areas of epidermal ulceration associated with hemorrhage (Fig.3D).

Leiomyosarcoma

Leiomyosarcoma was diagnosed in two samples of uterus (biopsies) obtained through hysterectomy in older females (median age of 21-months old). Histologically, these were characterized by a highly cellular neoplastic proliferation of spindle cells arranged in bundles in multiple directions, with moderate amounts of eosinophilic and poorly limited cytoplasm, and moderate pleomorphism.

Ovarian granulosa cell tumor

Ovarian granulosa cell tumor was diagnosed in two cases assessed as biopsies of the ovaries of two older females (median age of 36-months old). Microscopically, there was proliferation of cells arranged radially, which were lined and surrounded by moderate amounts of fibrous stroma, forming follicle-like structures.

Other neoplasms

Other neoplasms were identified individually, accounting for 2.5% (1/40) of the total of cases each: hepatoid gland adenoma, solid thyroid carcinoma, cutaneous melanoma, ovarian teratoma, and cutaneous trichoblastoma. Among these, ovarian teratoma was associated with the death of a 12-months old female Chinese hamster, while the other cases were diagnosed through biopsy. The ovarian teratoma featured an oval white mass occupying almost the entire abdominal cavity at the necropsy, measuring 5 × 3 × 3cm. This mass originated from the left ovary and displaced/compressed most of the abdominal cavity organs (Fig.3E). On the cut surface, it was predominantly soft, intermixed with firm to hard areas. Microscopically, the neoplasm was composed of cells of distinct germinative lines: epithelial, mesenchymal, and neuronal. The neoplastic cells formed multifocal random areas of stratified epithelium containing keratin, cartilaginous tissue, mineralized bone tissue, dentigerous tissue, muscle fibers, adipose tissue, glandular epithelium, and nervous tissue, which were intermixed with multifocal areas of necrosis (Fig.3F).

DISCUSSION

The diagnosis of neoplastic lesions in 40 hamsters in the present investigation was mainly based on the samples' gross and microscopic features, which were obtained either through anatomopathological or necropsy examination. Some factors, such as age range and sex predisposal, have been previously analyzed compared to the frequency and type of neoplasm detected, but there are still some controversies in the literature, as neoplasms tend to occur mostly in older hamsters, with an incidence of 70% reported in animals older than 2 years (Van Hoosier & Trentin 1979). Considering that hamsters may have a life span of 18- to 36-months old (Kamino et al. 2001, Kondo et al. 2008, Lennox & Bauck 2012), the hamsters of the present study were relatively younger with a median age of 14-months old, differing from a previous study wherein 19.8-months old was the median age of domestic hamsters affected by neoplasms. Male hamsters have been previously considered more prone to neoplasm development (Kamino et al. 2001, Kondo et al. 2008). However, another study conducted on Syrian control hamsters found a higher incidence of tumors in females (McInnes et al. 2013), similar to the current investigation. Previous studies focusing on spontaneous neoplasms have described these conditions mostly in Djungarian and Syrian hamsters (Kamino et al. 2001, Kondo et al. 2008, McInnes et al. 2013). In the present work, however, most of the neoplasms were detected in Chinese hamsters, possibly associated with the increasing popularity of the species as pet hamsters in Brazil (Conrado et al. 2013, Conceição et al. 2018).

Among the neoplasms detected, most of them (60%) involved the integumentary system, as observed previously in an investigation of spontaneous neoplasms in domestic Djungarian hamsters (Kondo et al. 2008). Similarly, a clinical retrospective study focused on hamsters' dermatological diseases observed that nodule formation (abscesses and neoplasms) was typical (White et al. 2019). It is believed that domestic hamsters are more affected by integumentary tumors when compared to laboratory specimens, wherein neoplasms tend to affect multiple organs (Kamino et al. 2001). In the present investigation, a higher level of cutaneous tumors may be related to the fact that SCC was frequently detected, accounting for 35% of the neoplasms. This differed from a previous study in which the primarily identified neoplasm was papilloma (Kondo et al. 2008), which was not detected in the present work, while SCC accounted for 8% of the cases in that study (Kondo et al. 2008). Nonetheless, other investigations conducted on Syrian laboratory hamsters reported a higher prevalence of spontaneous adrenal neoplasms (Kamino et al. 2001, McInnes et al. 2013). However, no adrenal gland neoplasm was identified in the current work, which could be related to the small number of Syrian hamsters in the analyzed population.

Squamous cell carcinoma (SCC) is relatively common in Syrian hamsters submitted as experimental models in research in order to evaluate chemical carcinogens effects at the buccal pouch, such as dimethylbenzanthracene (DMBA) or carbamide peroxide (De Oliveira et al. 2009, Bampi et al. 2014). The buccal pouch is the primary location for chemical carcinogenesis studies in hamsters because of the low cost and easy anatomical access, which can be readily everted for gross evaluation (Mognetti et al. 2006). Nonetheless, the spontaneous occurrence of the condition is poorly described, with most of the reports focused on the cheek pouch (Martorell et al. 2005, Ghaffari et al. 2009, Capello 2011), while the involvement of lips, gingiva, mandible, and maxilla, as detected in the current investigation, is relatively uncommon (Conceição et al. 2018). The hamsters affected in the present work had an age range of 8- to 24-months old, with a median age of

12-months old, which are data quite similar to those previously reported in other studies (Ghaffari et al. 2009, Conceição et al. 2018). Djungarian, Chinese, and Syrian hamsters appear to be equally susceptible to SCC development (Martorell et al. 2005, Ghaffari et al. 2009, Conceição et al. 2018). Although the current study did not detect any SCC in Syrian hamsters, this is possibly related to the small number of rodents from this species analyzed in the current work.

Squamous cell carcinoma (SCC) development in other domestic species is often related to ultraviolet light chronic exposure, lack of skin pigment, and scarcity or absence of hair at the sites affected (Goldschmidt & Goldschmidt 2017). Although hamsters are nocturnal rodents usually maintained in environments where sunlight exposure is minimal (Martorell et al. 2010), these factors were most likely associated with SCC occurrence in the present investigation, as non-pigmented regions and areas less covered by hairs were mostly affected, such as lips, nasal region, and ears. The oral region has also been identified as a common location for SCC development in adult African pigmy hedgehogs (*Atelerix albiventris*) (Aguila et al. 2019) and the second most common in the oral cavity of dogs, while in cats, it mainly involves the facial and nasal regions (Goldschmidt & Goldschmidt 2017). In the lips, the condition usually begins as erythematous, squamous, and, often, ulcerative lesions that progress to highly infiltrative masses, which are rarely able to metastasize (Gardner 1996). Similarly, no metastases were detected in the hamsters of the present study at the regional lymph nodes. It is presumed that death was mostly related to the neoplasm's infiltrative behavior, which was able to cause facial deformities and dysphagia, similarly to that described in Chinese and Syrian hamsters in other studies (Ghaffari et al. 2009, Conceição et al. 2018). This pathogenesis is similar to that reported in African pigmy hedgehogs affected by oral SCC, in which masses diagnosed as SCC caused facial deformation, dysphagia, and infiltration of the nasal cavity induced characteristic clinical signs (Aguila et al. 2019). Considering that many pet rodents are experts in hiding signs of illness and those pet hamsters are less likely to be presented for veterinary treatment with spontaneous tumors than other small rodents, the diagnosis of unusual diseases is often reduced or retarded (Greenacre 2004, Ghaffari et al. 2009, Rainwater et al. 2011). Additionally, pursue diagnostic investigations in hamsters is often constrained by economic reasons, as owners are inclined not to spend money on a small rodent with a short life span (White et al. 2019), and, therefore, these animals usually do not undergo full gross and histopathologic examinations (Rainwater et al. 2011). Thus, the current study highlights the importance of SCC early diagnosis because out of eight hamsters submitted to necropsy; five died promptly after or during surgical resection of the mass.

Lymphoma was the second most common neoplasm in this investigation, and, similarly, the occurrence of the condition has been extensively reported in hamsters, (Van Hoosier & Trentin 1979, Coggin et al. 1983, Harvey et al. 1992, De Alencar et al. 2012). In another study conducted with laboratory hamsters, lymphoma prevalence reached 8% (Kamino et al. 2001), which is quite similar to the frequency observed in this study (10%). Lymphoma involvement in the species is usually referred as multicentric, because multiple organs may be affected simultaneously. Peripheral and visceral lymph nodes are the primary sites affected (Santos et al. 2002), as in the current work. Nonetheless, the small intestine and liver are also commonly involved (Santos et al. 2002, Coggin et al. 1983), as observed. The liver was affected in two cases and the small intestine in one case. Other organs inflicted may include the spleen, kidneys (Santos et al. 2002), and mediastinum (thymus) (Coggin et al. 1983), which were also affected in this study. Grossly, lymphoma usually presents as soft, round, yellow-white masses, often with central necrosis, involving the lymph nodes, liver, and kidneys (Coggin et al. 1983), as observed in this investigation. On the other hand, spleen and hepatic involvement are characterized by diffuse enlargement (splenomegaly) and whitish foci within the parenchyma (Coggin et al. 1983), similar to the present work.

Histologically, lymphomas may be classified into multiple histological and phenotypical patterns, being large cell lymphoma the most common pattern in Syrian hamsters (Santos et al. 2002). Accordingly, the cases of the present work were classified as high grade diffuse large cell lymphomas. Additionally, lymphomas in hamsters generally contain conspicuous amounts of karyorrhectic debris and tingible bodies within histiocytic cells, which indicates a "starry sky" morphologic appearance (Coggin et al. 1983) similarly to the cases in the current investigation. Multicentric lymphoma may be induced by hamster polyomavirus (HaPV), a Papovaviridae virus, in young Chinese and Syrian hamsters during outbreaks of HaPV (Coggin et al. 1983, Simmons et al. 2001). In the present study, we could not assert if HaPV was involved in the cases detected, as all samples were already paraffin-embedded and, thus, molecular detection was not performed. Nevertheless, considering that lymphoma affected hamsters with a median age of 19-months old in this study, a viral etiology is less likely for these cases because HaPV infection is related to lymphoma in young hamsters (5-weeks old). In contrast, older animals usually develop immune resistance to lymphoma development (Coggin et al. 1983). Additionally, lymphoma induced by HaPV infection mostly occurs in research colonies (Hocker et al. 2017), but rarely in pet hamsters (Simmons et al. 2001).

Fibrosarcomas often have an infiltrative and recurrent behavior, but metastases are rare in domestic animals (Hendrick 2017), similarly to the present study wherein single nodules restricted to the skin were observed. These lesions involved mainly the limbs and ventrum (mammary gland), which are referred as the most common locations for fibroma or fibrosarcoma development in hamsters (Kondo et al. 2011, Hocker et al. 2017). Differential diagnosis of fibrosarcoma in hamsters should include atypical fibroma/fibrosarcoma, a neoplasm derived from ganglion cell-like (GL) cells characterized by large amounts of GL cells, which are similar to histiocytes or neurons and intermixed with collagen fibers (Baba et al. 2003). Considering that GL cell levels in the dermis and subcutaneous tissue is dependent on circulating androgen levels, most atypical fibromas are detected in sexually mature male hamsters older than 7-months (Hocker et al. 2017), while most of the cases of the present work occurred in females. Additionally, the cases herein were differentiated through the neoplastic cells' histological features, as these were predominantly spindle. At the same time, atypical fibromas/fibrosarcomas present polygonal to angular to spindle-shaped and medium-large neoplastic cells, as well as large amounts of collagen fibers (Kondo et al. 2011). Moreover, extraskeletal osteosarcoma should

also be considered a differential in these cases, as previously reported in a one-year old Chinese hamster (Conrado et al. 2013) and this was obtained by the absence of osteoid within the neoplasms diagnosed.

When mammary tumors are examined, only benign neoplasms corresponding to mammary cystadenomas were identified. Similarly, in rats, mammary tumors are mostly composed of benign mammary fibroadenomas, which rarely metastasizes, and, thus, surgical treatments are related to good prognosis (Capello 2011), as in the present study wherein all samples were obtained through biopsies and were not related to death in the affected hamsters. Mammary tumors are widely reported in hamsters, with adenoma and adenocarcinoma identified as the most frequent (Kondo et al. 2009). A genetic predisposal was suggested in Djungarian hamsters (Jelinek et al. 2013). Despite the report of other studies of the occurrence of mammary tumors solely in Djungarian hamsters (Kamino et al. 2001, Kondo et al. 2009, Jelinek et al. 2013), this study identified the neoplasm in Syrian and Chinese hamsters as well. Besides, a previous study identified that mammary adenomas accounted for 12% of the neoplasms in domestic hamsters (Kamino et al. 2001), which is similar to the present study's frequency (10%). Moreover, young hamsters with a median age of 12-months old were mostly affected in the present investigation, similarly to previous studies (Kamino et al. 2001, Yoshimura et al. 2015).

The reproductive system was the second most commonly affected in this study, after skin neoplasms. These systems are the most commonly involved in surgical procedures in both female and male rodent patients. Ovariohysterectomy may be recommended in females to prevent reproductive disease, such as mammary tumors, or as a therapeutic measure in debilitated animals (Capello 2011). In the present work, reproductive tumors were represented mostly by mammary neoplasms, followed by uterine and ovarian neoplasms, such as leiomyosarcoma, ovarian granulosa cell tumor, and teratoma. Although uterine tumors are widely described in laboratory animals and leiomyomas are regarded as the most common uterine neoplasms in hamsters (Kamino et al. 2001), two uterine cases of leiomyosarcoma were diagnosed in the present study. Differential diagnosis should rely on tumoral pleomorphism and mitotic index (Kondo et al. 2007), as performed in the current investigation. Other differentials include uterine adenocarcinomas (Kamino et al. 2001) and collision tumors with mixed granular cell tumor and uterine adenocarcinoma (Golbar et al. 2011), which was obtained through the microscopical features of the neoplasm. Uterine tumors are common in aged hamsters (Kamino et al. 2001, Golbar et al. 2011), similar to the present study, wherein the animals had a median age of 21-months old.

A considerable high incidence of ovarian granulosa cell tumor was previously detected in approximately 25-month old female laboratory hamsters (McInnes et al. 2013), similarly to the present study in which the two females affected by this neoplasm were 36-months old. Moreover, we report a novel case of ovarian teratoma in a Chinese hamster, and, although it has not been previously detected as a spontaneous neoplasm in domestic hamsters (Kondo et al. 2008), it may be induced in male Syrian hamsters through intratesticular inoculation of zinc chloride (Guthrie & Guthrie 1974). Ovarian teratomas are rare neoplasms in domestic animals and are originated from pluripotent germ cells of the ovaries or testicles, being mostly described in dogs and horses. These cells may differentiate into multiple tissues, such as bone, cartilage, teeth, or skin and its adnexa (Agnewl & Maclahlan 2017), as observed in the present case. Most teratomas are benign tumors, but some tissue components may have malignant features (Agnewl & Maclahlan 2017). In the present study, however, no malignant feature of metastasis was identified.

CONCLUSIONS

Neoplasms are important causes of death or a major reason to perform biopsy in domestic hamsters in Southern Brazil. The hamsters affected in this study had a median age of 14-months old, and females were slightly more affected than males.

Cutaneous neoplasms were most commonly identified, and Squamous cell carcinoma (SCC) was the most frequent tumor, wherein the lip/nasal region was mostly affected. Other identified neoplasms included lymphoma, fibrosarcoma, and mammary cystadenoma, in addition to less common neoplasms, such as uterine leiomyosarcoma, ovarian granulosa cell tumor, and ovarian teratoma.

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Animal welfare/ethical statement.- We authors of the article entitled "Neoplasms in domestic hamsters in Southern Brazil: epidemiological and pathological aspects of 40 cases" declared, for all due purposes, the project that gave rise to the present data of the same has not been submitted for evaluation of the Ethics Committee of the "Universidade Federal do Rio Grande do Sul" (UFRGS), but we are aware of the content of the Brazilian resolutions of the "Conselho Nacional de Controle de Experimentação Animal (CONCEA)" <http://www.mct.gov.br/index.php/content/view/310553.html> if it involves animals. Thus, the authors assume full responsibility for the presented data and are available for possible questions, should they be required by the competent authorities.

Conflict of interest statement.- The authors have no competing interests.

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