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CASE REPORT
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Primary Intestinal Fibrosarcoma in Cats

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ABSTRACT

***Background*:** Fibrosarcomas are malignant neoplasms of mesenchymal origin and can have different symptoms depending on the species, age, location and etiopathogenesis. Intestinal tumors in domestic cats are common and the small intestine is the most common site; however, fibrosarcomas are rare in the intestine of all animal species. This work reports intestinal fibrosarcoma in 2 domestic cats and aims to clarify and present information concerning this neoplastic type in the gastrointestinal tract of this species.

***Cases*:** We report 2 cases of intestinal fibrosarcoma in domestic felines (*Felis catus*). Cat 1. A 14-year-old female Persian breed, domestic cat, was taken to the Feline Sector of the Veterinary Hospital of Small Animals (HVPA) of the Federal Rural University of Rio de Janeiro (UFRRJ). The main complaint was chronic constipation and rectal prolapse. The clinical examination revealed an ulcerated mass, measuring 4.0 cm x 1.7 cm. *Cat 2*. A 10-year-old female undefined breed, domestic cat, was taken to the private clinic. The main complaint was diarrhea with bloody and rectal prolapse. The clinical examination revealed nodule measuring 2.5 cm in diameter. The surgical option decided upon was to use the rectal pull-through technique in both animals. The patients had no trans-surgical or postoperative complications. The material collected during the surgical interventions was analyzed macroscopically and fixed in 10% buffered formalin for 24 h and then sent to the Histopathology Laboratory of the Pathological Anatomy Sector (SAP) at UFRRJ for the *cat 1* and in private laboratory for the *cat 2*. After fixation, it was cleaved for routine microscope exam using Hematoxylin and Eosin (HE) stains and for the histochemical method of Masson's Trichrome staining technique. Complementary immunohistochemistry tests and electron microscopy were also performed. The patients were followed up clinically, showing complete remission of the clinical signs and survival for approximately 1 year after the neoplastic resection.

***Discussion*:** There are few reports of intestinal fibrosarcomas in veterinary medicine, therefore, little is known about racial predilection, age, sex or biological behavior. As far as these authors know, this is the 6th and 7th report of this neoplasm with a primary site in the large intestine in this species. The morphological diagnosis of fibrosarcoma is relatively simple, whereas, in some cases the differential diagnosis for tumors of the peripheral nerve sheath, leiomyosarcomas and gastrointestinal stromal tumor (GIST) can be extremely difficult. The immunohistochemistry technique in these cases may not be particularly useful. The fibrosarcoma diagnosis was also confirmed by electron microscopy since no evidence was found that could lead to a neuronal origin, thus excluding tumors such as neurofibrosarcoma and schawnoma, corroborating the immunohistochemical examination. The surgical management of tumor resection with wide safety margins (minimum 2 cm) remains the "gold standard" therapy for dealing with fibrosarcomas since they have a low response rate to chemotherapy and radiotherapy and the use of these therapies as an adjuvant is controversial. The advantages of this technique are related to the surgical time, simplicity, easy access and reduction in the risk of abdominal contamination. Histopathological, immunohistochemistry and electron microscopy evaluations were sufficient to enable the diagnosis of an intestinal fibrosarcoma in both cats. The occurrence of this neoplasm with intestinal involvement in the feline species is rare; therefore, this description is important as it provides information about epidemiology, associated signs, differential diagnoses, biological behavior, treatment and prognosis.

Keywords: feline, intestine, mesenchymal, tumors, neoplasm, rectal pull-through.

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INTRODUCTION

Fibrosarcomas are malignant neoplasms of mesenchymal origin that can have different symptoms depending on the species, age, location and etiopathogenesis [6,13]. They are defined as sarcomas derived from fibroblasts or microfibroblasts [10]. Fibrosarcomas are neoplasms commonly reported in medicine with a primary site in soft tissues and in elderly individuals [3]. In veterinary medicine they have a high occurrence in adult domestic animals and are more common in subcutaneous tissue [9].

Fibrosarcomas in domestic cats at the subcutaneous site are often associated with vaccine-associated sarcoma, which are commonly seen in the thorax, lumbar, flank and limb regions. Infiltrative tumors are often recurrent in their primary sites; however, metastases are uncommon [13].

Intestinal tumors in domestic cats are common and the small intestine is the most common site [15]. These can cause clinical signs such as obstruction and intestinal dysfunction, in addition to ulceration, perforation, and septic peritonitis [13,16]. Among these neoplasms regularly diagnosed are lymphoma, followed by adenocarcinoma and mastocytoma. Fusocellular sarcomas have a lower occurrence in the gastrointestinal tract, where leiomyosarcoma is the most described one; however, fibrosarcomas are rare in the intestine of all animal species [13].

Fibrosarcomas have a low response rate to chemotherapy and radiotherapy, and surgical resection with a wide safety margin is considered the treatment of choice for this tumor type [8,12].

This work reports intestinal fibrosarcoma in 2 domestic felines (*Felis catus*) and provides data regarding this neoplastic type affecting the gastrointestinal tract in this species.

CASES

Cat 1. A 14-year-old female, domesticated, neutered, Persian cat was seen at the Domestic Cats Medical Clinic at the Veterinary Hospital of Small Animals (HVPA) of the Federal Rural University of Rio de Janeiro (UFRRJ). The main complaint was chronic constipation and prominence of part of the intestine beyond the rectal orifice. The clinical examination reported an ulcerated mass of 4.0 cm x 1.7 cm in the rectum region (Figure 1A). Ultrasonographic examination revealed a slightly irregular, hyperechoic nodule, with a poorly defined edge in the colon region of about 3.0 cm, however, there was no increase in the mesenteric and iliac lymph nodes.

Cat 2. A 10-year-old female undefined breed, domestic cat, was taken to the private clinic. The main complaint was diarrhea with bloody and rectal prolapse. The clinical examination revealed nodule measuring 2.5 cm in diameter (Figure 1B).

The surgical treatment of choice was the complete rectal "pull-through" technique [8]. Repair sutures positioned at the mucocutaneous junction in the rectum region were performed to draw the tumor out caudally with the aid of 2-0 polyamide thread[1] and a 360-degree incision was made around it (Figure 1C). Subsequently, the rectal segment was dissected cranially, and its vessels connected to the final portion of the descending colon. In order to assure a wide

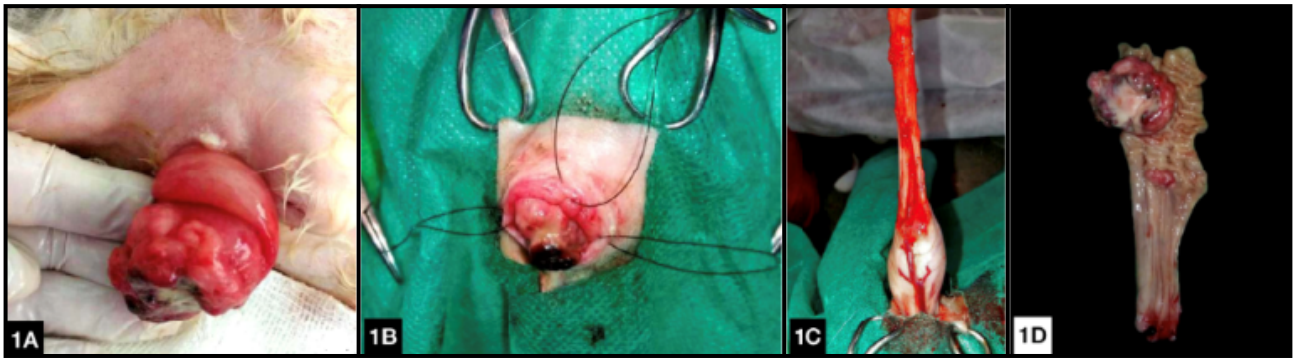

Figure 1. Complete rectal "pull-through" technique in a 14-year-old female, domesticated, neutered, Persian cat (*cat 1*) seen at the Domestic Cats Medical Clinic at the Veterinary Hospital of Small Animals - UFRRJ. A- Feline showing prolapse of rectum with a mass measuring 3.5 x 2.5 cm along its longest axis in the region of the rectum. B- Pull-through technique: repair sutures in the rectum placed at the mucocutaneous junction, using 2-0 polyamide thread. C- Pull-through technique: rectum dissected cranially, and the rectal vessels connected in the final portion of the descending colon. D- Final portion of large intestine sectioned longitudinally: presence of 2 masses measuring 3.5 x 2.5 cm and 1.0 x 0.6 cm, of firm elastic consistency with a whitish coloration and change in the mucosa pattern between the rectum and the descending colon.

surgical safety margin from the masses, the rectum was transected in stages, so that at each transection of the rectal mucosa was sutured to the mucocutaneous junction until the entire exposed rectal portion was resected and sutured using 3-0 polypropylene thread[1] (Figure 1D). In this way, a surgical resection of a segment of approximately 15 cm from the rectum and the distal part of the descending colon was made in order to obtain margins free of the neoplastic process.

The material collected during the surgical intervention was analyzed macroscopically and then fixed in 10% buffered formalin[2] for 24 h and sent to the Histopathology Laboratory of the Pathological Anatomy Sector (SAP) at UFRRJ for the *cat 1* and private laboratory for *cat 2*. At the laboratory, it was fixed and cleaved for routine microscope exams using Hematoxylin[3] and Eosin[3] (HE) dyes for both cases and for the Masson's Trichrome[3] staining histochemical technique for *cat 1*.

Complementary immunohistochemistry tests were performed for both cases using the vimentin antibody[3] at the UFRRJ SAP Immunohistochemistry Laboratory. Silanized slides with serial slices of the masses were prepared for these exams. A lymph node fragment was used as the positive control. The histological sections were dewaxed in 2 xylol baths (20 min each), hydrated in 4 alcohol baths (5 min each) and incubated for 15 min in freshly diluted 3% hydrogen peroxide. Then, after a 2nd dilution to block endogenous peroxidases the sections were left for a further 15 min in this solution. After this the slides were washed with distilled water, and then placed in a water bath with Tris buffer (pH 9.0) at approximately 98ºC for 15 min for antigen recovery. Nonspecific reactions were blocked with 5% skimmed milk[4] for 30 min. The sections were incubated "overnight" with vimentin antibody (monoclonal) at a 1:100 dilution (1 µL of antibody to 100 µL of PBS or ADS-125 Antibody Diluent). The REVEAL polymer-HRP detection system was used, free of biotin (Spring) and as a chromogen to diaminobenzidine (DAB). All sections were counterstained with Harris hematoxylin and then evaluated under an optical microscope[5] and photographed using a digital microscope camera[6].

In order to verify with the antibody panel[3] of alpha smooth muscle actin, desmin, CD56, S100, Factor VII and CD117, a paraffin block with a fragment of the neoplasia was sent to a private laboratory. An electron microscopy exam was also performed with tumor fragments that were sent to the Animal Pathology Laboratory at the University of Minnesota in the USA in order to try to elucidate the origin of the neoplasm.

The macroscopic evaluation for both cases showed two nodular lesions with an elevated surface and an irregular shape, measuring 3.5 x 2.5 cm; 1.0 x 0.6 cm and 2.2 x 2.1 cm; 2.0 x 1.1 cm along their major axes for *cats 1* and *2* respectively. They were located in the intestinal mucosa between regions of the rectum and the descending colon (Figure 1D). Both were of firm-elastic consistency and had a predominantly whitish coloration with reddish areas, and changes in the mucosa pattern. For the *cat 2* showed 2 nodular lesions

The felines did not present postoperative complications. The stitches were removed 20 days after the surgical procedures and was discharged.

The histopathological examination of both animals revealed an infiltrative proliferation of spindle to ovoid shaped neoplastic cells, extending from the mucosa to the submucosa, sometimes arranged in the form of a mantle and sometimes arranged in bundles. There was moderate anisocytosis and anisokaryosis, with evident nuclei that were sometimes multiple, and dense chromatin. Mitosis figures were frequent and, for the most part, were atypical (Figure 2A & B). Based on the microscopic analysis, the diagnosis established was poorly differentiated fusocellular sarcoma.

A fragment of neoplastic tissue in a paraffin block was sent for a more accurate evaluation with an immunohistochemical panel. Both cases had the same immunohistochemical profile regarding positive and negative tumor cell markers. The result was strongly positive for the vimentin antibody (Figure 3A), whose expression is observed in cells of mesenchymal origin, and negative for the alpha actin (Figure 3B) and desmin markers, with expression in smooth muscle; CD56, antibody for the adhesion molecule of neural and neuroendocrine cells; S100 (Figure 3C), marker of neuroglial, ependymal, and melanocytic cells as well as Schwann cells and Factor VIII, antibody to endothelial cells. Furthermore, there was no immunoreactivity to CD117, an antibody expressed in gastrointestinal stromal tumors (GIST). Although there is no specific antibody for this neoplasia, the results of the immunohistochemical panel suggested the diagnosis of fibrosarcoma by exclusion. Table 1 summarizes the individual results for the markers used.

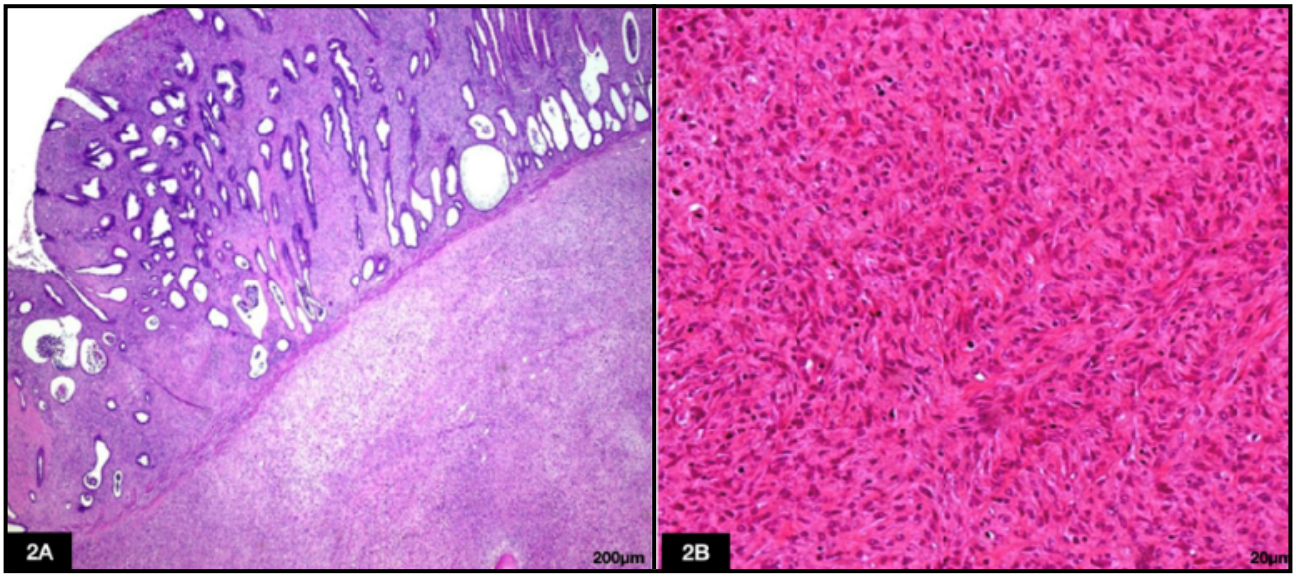

Figure 2. Histopathological features observed in the intestinal tumor of a 14-year-old female, domesticated, neutered, Persian cat (*cat 1*) seen at the Domestic Cats Medical Clinic at the Veterinary Hospital of Small Animals - UFRRJ. A- Histological section of the intestine showing infiltrative proliferation of spindle-shaped neoplastic cells arranged in bundles extending from the mucosa to the submucosa [HE; 4x]. B- Histological section showing cells of fusocellular morphology with moderate pleiomorphism and anisocariosis [HE; 40x].

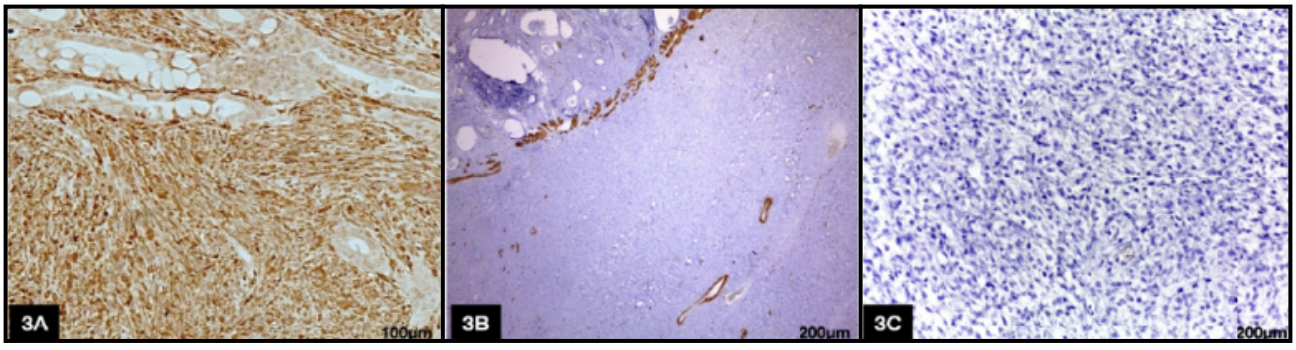

Figure 3. Immunohistochemical profile of intestinal tumors of a 14-year-old female, domesticated, neutered, Persian cat (*cat 1*) seen at the Domestic Cats Medical Clinic at the Veterinary Hospital of Small Animals - UFRRJ. A- Immunohistochemical panel positive for the vimentin antibody [10x]. B- Negative immunohistochemical panel for the alpha actin antibody [4x]. C- Immunohistochemical panel negative for the S-100 antibody [40x].

Table 1. Individual results of the markers used in the intestinal tumors of both felines (cats 1 and 2) reported in this study.

Antibodies		Clone	Result
Vimentin	Cells of mesenchymal origin	Monoclonal	Positive in the neoplastic cells
Alfa Smooth Muscle Actin	Cytoplasmic myofilaments with expression in smooth muscle, myoepithelial cells and myofibroblasts	1A4	Negative in the neoplastic cells
Desmin	Intermediate filament of muscle cells	D33	Negative in the neoplastic cells
CD56	Adhesion molecule of neural and neuroendocrine cells	BC56C04	Negative in the neoplastic cells
S100	Marker for neuroglial, ependymal, and melanocytic cells and Schwann cells	Polyclonal	Negative in the neoplastic cells
Factor VIII	Marker for endothelial cells	Polyclonal	Negative in the neoplastic cells
CD117	Proto-oncogene C-KIT or protein tyrosine kinase c-kit	Polyclonal	Negative in the neoplastic cells

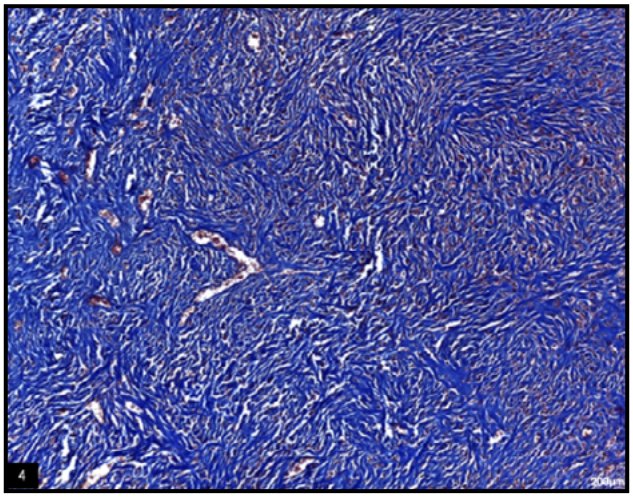

Figure 4. Histochemical method for staining Masson's Trichrome a 14-year-old female, domesticated, neutered, Persian cat (*cat 1*) seen at the Domestic Cats Medical Clinic at the Veterinary Hospital of Small Animals - UFRRJ, with positive marking on cells from connective tissue [40x].

In order to reinforce the histochemical diagnosis of fibrosarcoma, Masson's Trichrome staining method was carried out, and here it was possible to see the positive blue tone in the cells coming from connective tissue, thus reinforcing the possibility that the neoplasia was of fibroblast origin (Figure 4).

In the electron microscopy analysis, elongated cells in a disorganized arrangement, euchromatic nuclei, evident nucleoli, and cytoplasm with low density of organelles were observed; however, there was no evidence of neuronal origin, thus, the diagnosis established was a soft tissue sarcoma (Figure 5A & B), which corroborates the immunohistochemical examination and strengthens the diagnosis of intestinal fibrosarcoma.

After the confirmation of the diagnosis of fibrosarcoma and verification that the surgical margins were free of tumor cells, a multidisciplinary medical group together with the tutor chose not to institute any chemotherapy treatment. The both cats attended followed up sessions for post-surgical revisions and there were no signs of tumor recurrence and/or complications associated with the surgical technique used during the 12-month and 4-month post-intervention period for cats *1* and *2* respectively.

DISCUSSION

There are few reports of intestinal fibrosarcomas in veterinary medicine, therefore, little is known about racial predilection, age, sex or biological behavior. In the canine species, 2 reports of intestinal fibrosarcoma have been reported [2]. In the retrospective study by Risseto *et al.* [15], with an epidemiological focus on intestinal neoplasms in cats over a 40-year period, only 5 cases of fibrosarcoma were reported and all in the large intestine. As far as these authors know, this is the 6th and 7th report of this neoplasm with a primary site in the large intestine in this species.

Cats with intestinal tumors are generally elderly, with an average age between 10.6 and 12.6 years old for gastrointestinal tumors and 8.7 and 12.3 years old for intestinal tumors. Mean ages of 11 to 11.8 and 12.5 years old have been reported for tumors of the small and large intestine, respectively [15]. In this report,

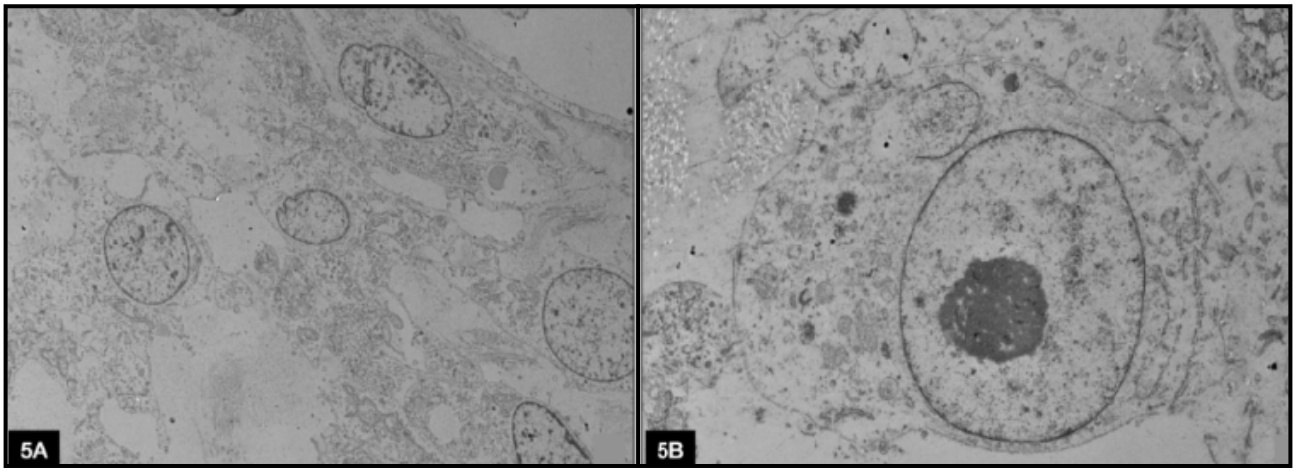

Figure 5. Electron microscopy analysis of intestinal tumors of a 14-year-old female, domesticated, neutered, Persian cat (*cat 1*) seen at the Domestic Cats Medical Clinic at the Veterinary Hospital of Small Animals - UFRRJ. A- Electron microscopy examination showing neoplastic cells with an elongated to polygonal morphology, in a disorganized arrangement, evident nucleoli and cytoplasm showing low density of organelles. B- Electron microscopy examination showing in more detail the neoplastic cells with an elongated to polygonal morphology, in a disorganized arrangement, evident nucleoli and cytoplasm showing low density of organelles.

the felines were senile in age as reported for intestinal neoplasms of different origins [13].

Sexual predilection is controversial in relation to feline intestinal tumors, in some studies, males were reported to be more affected, while others reported an equal representation between the genders [15]. Siamese, on the other hand, are the most affected breed and there have been no reports of this type in Persian cats, until now [15,17].

The vast majority of the data found in the literature regarding the predilection and behavior of fibrosarcomas refers to subcutaneous sites; there is no special further information concerning the intestinal types due to their rarity. In the current study, the neoplasm showed infiltrative behavior in the intestinal mucosa and macroscopic characteristics similar to those observed in other primary sites [13].

The morphological diagnosis of fibrosarcoma is relatively simple, whereas, in some cases the differential diagnosis for tumors of the peripheral nerve sheath, leiomyosarcomas and gastrointestinal stromal tumor (GIST) can be extremely difficult [13]. The immunohistochemistry technique in these cases may not be particularly useful, since all these tumors are positive for the vimentin antibody, and the positivity of S100 is notoriously nonspecific [11,13]. However, in the cases of differentiation for leiomyosarcoma and GIST, both of which are fusocellular tumors and they are found in intestinal sites, so the positive marking of the cytoplasm of neoplastic cells for the antibodies actin/desmin and CD117, would evidence the origin of smooth muscle and GIST respectively, thus these principal differential diagnoses were excluded. As none of the immunomarkers showed a positive reaction to staining, except vimentin, which was extremely positive, the histological diagnosis of a primary intestinal fibrosarcoma is confirmed.

The electron microscopy examination also helped diagnose fibrosarcoma. The results of the immunohistochemical panel were negative for antibodies and therefore, this excludes their main differentials. Thus, the diagnosis was carried out by exclusion, since there is no specific antibodies to perform and confirm the technique through immunohistochemistry. Furthermore, the fibrosarcoma diagnosis was also confirmed by electron microscopy since no evidence was found that could lead to a neuronal origin, thus excluding tumors such as neurofibrosarcoma and schawnoma, corroborating the immunohistochemical examination.

The surgical management of tumor resection with wide safety margins (minimum 2 cm) remains the "gold standard" therapy for dealing with fibrosarcomas since they have a low response rate to chemotherapy and radiotherapy and the use of these therapies as an adjuvant is controversial [8,12]. The rectal pull-through technique is described in the literature as an option for the resection of distal rectal lesions in dogs and cats, allowing surgical access without the need for pubic osteotomy [1]. The advantages of this technique are related to the surgical time, simplicity, easy access and reduction in the risk of abdominal contamination [4]. In contrast, the rectal pull-through technique is also related to high rates of postoperative complications, with fecal incontinence being the most frequent [1,14]. In the present report, the use of this technique was satisfactory, allowing quick and simple access to the region where the tumors were located, respecting the surgical safety margin, without postoperative complications and thus a quick return to the animal's quality of life. Furthermore, the surgical team involved in this report chose not to perform excision of the satellite lymph nodes, since they did not present any changes in the ultrasound images, a conduct that was ratified after the diagnosis of the tumor, since less than 5% of the sarcomas cause metastasis to the lymph nodes [7].

Despite the diagnosis of a poorly differentiated fibrosarcoma (high grade) in the felines of the present study, the decision was made not to perform any adjuvant therapy since the surgical safety margin was maintained, the clinical signs were remitted, the cat was elderly and upon request of the tutor. The histopathological grading is the most important prognostic factor to be considered in patients with fibrosarcoma [5], however, due to its aggressive nature, the overall survival rate of these patients is low in human medicine [3] while little is known in veterinary medicine [2]. Avci *et al.* [2] reported a case of an 11-year-old dog with fibrosarcoma in the jejunum region, which was excised using the enterectomy procedure with a surgical safety margin and end-to-end enteroanastomosis, with the animal being accompanied for 6 months, showing no signs of recurrence or tumor metastasis during that period. In the present report, the cat had a 1-year survival, when euthanasia was chosen due to a possible neoplasia of unclear origin.

Due to the rarity of information on enteric fibrosarcomas in felines, especially when the

involvement occurs at the level of the large intestine, further studies are needed to show the behavior of this type of neoplastic located in this region so that the clinical management for the treatment and prognosis of this condition is better understood.

The histopathological, immunohistochemical and electron microscopy evaluations enabled the diagnosis of intestinal fibrosarcoma in 2 cats. The occurrence of this neoplasm with intestinal involvement in the feline species is rare, therefore, this description is important as it provides data about its epidemiology, associated clinical signs, differential diagnoses, biological behavior, treatment and prognosis.

MANUFACTURERS

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***Declaration of interest*.** The author reports no conflicts of interest. The authors are responsible for the content and writing of paper.

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