Feline restrictive orbital myofibroblastic sarcoma: a clinical case and review of the literature

The clinical history of an 8-year old, Domestic Shorthair, spayed female cat, affected by feline restrictive orbital myofibroblastic sarcoma (FROMS) is re-examined, from the first ophthalmological assessment, with exophthalmos, absent palpebral motility and exposure keratitis of the right eye, to the contralateral and oral extension of the tumour and death induced, 10 months later, by euthanasia. Results of the investigations (blood-chemistry tests, imaging, neurological examination, dental examination) and follow-up are presented, together with a review of the literature, in order to provide details about the pathogenesis of this unusual feline neoplasm with the purpose of improving the diagnosis and prognosis of affected patients in the future.

Key words - Froms, orbit, feline, exophthalmos.

INTRODUCTION

Feline restrictive orbital myofibroblastic sarcoma (FROMS) is a clinical condition characterised by exophthalmos and reduced motility of the eyelids and globe, resulting in exposure keratitis, with a tendency to extend to the contralateral orbit and adjacent structures (eyelids, nictitating membrane, glandular tissue, oral cavity, nasal submucosa)\(^1\)\(^2\)\(^3\)\(^4\).

The initial presentation of FROMS is often subtle and the condition can be confused with other orbital (abscesses, cellulitis, other tumours, cystic lesions), neuro-ophthalmological or corneal problems (herpesvirus keratitis)\(^4\).

Given that FROMS is an invasive tumour, which responds poorly, if at all, to attempted medical therapy and that tendentiously it has a poor long-term prognosis\(^1\)\(^2\)\(^5\)\(^6\), it is essential to recognise this condition early and to start aggressive therapy immediately in order to prevent the involvement of other tissues, if possible.

Despite the severity of this condition, little is yet known about its pathogenesis and possible underlying causes. Here we describe the clinical history of a case of FROMS and review the currently available literature on the subject, including the still limited number of cases that have been reported, in order to provide new clinical data useful for the diagnosis and understanding of this disease.

CASE REPORT

History

A Domestic Shorthair, spayed female cat, about 8 years old, was brought to the Specialist Veterinary Centre (Rome) for an ophthalmological evaluation because of a greyish patch on the cornea of the right eye (OD - oculus dexter), which had been present for a few days. The owner reported, as the only relevant fact in the past medical history, that at the age of about 4 months, the cat had had a head injury which had caused a perma-

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ent deformity of the left side of the skull and psychomotor seizures.

**Physical examination**

The right orbit appeared exophthalmic with marked resistance to retropropulsion, absence of eye movements and inability to blink. The surface of the cornea between the palpebrae of the OD showed a dry-looking, elliptical area, with a longer horizontal axis, which stained positively with fluorescein (Fluorescein; Haag-Streit AG, Koeniz, Switzerland). The cornea of the left eye (OS - oculus sinister) was apparently normal. Direct and consensual pupillary light reflexes were normal bilaterally (OU - oculus uterque), while the menace response and dazzle reaction were positive OS and negative OD. The blink reflex and corneal reflex were present and normal OS while they were absent on the right side. The Schirmer Tear Test I (STT; Standardized Sterile Stripes; Schering-Plough Animal Health, Union, USA) was 15 mm/min OS while it was not carried out on the right eye because of lack of access to the conjunctival fornix. After topical application of anaesthetic eye drops (benoxinate hydrochloride, Benoxinate Hydrochloride Intes; Alfa Intes, Casoria, Italy) intraocular pressure was measured by an applanation tonometer (Tono-Pen® VET; Reichert Technologies, New York, USA) and found to be 17 mmHg (OD) and 24 mmHg (OS) (reference values: 19.7 ± 5.6 mmHg). There was anisocoria with mild miosis of the right eye. By semi-quantitative measurement, aqueous flare was assessed as 0 (OS) and 1+ (OD) on a scale from 0 to 4+. Following pharmacological dilatation with tropicamide-based eye drops (Visumidria 1%; Visufarma, Rome, Italy), indirect ophtalmoscopy (Heine OMEGA® 500; Heine, Herrsching, Germany) of the fundus revealed an indented area in the dorsolateral part of the globe. The response to pharmacological dilatation unmasked slight resistance to pupillary dilation OD. The ocular structures on the left eye were within the norm. Exploration of the oral cavity, performed without causing the patient obvious pain, revealed appreciable gingival inflammation with eroded-ulcerated areas around the last premolar and the first molar of the right maxillary arch.

**Differential diagnosis**

On the basis of the clinical picture, the preliminary diagnosis was a retrobulbar mass with secondary corneal ulcers and reflex uveitis OD. Possible differential diagnoses included a neoplastic lesion, FROMS, retrobulbar orbital abscess or cellulitis. The presence of a lesion in the post-chiasmatic visual pathway was also suspected (menace response and dazzle reflex absent OD). Possible involvement of the VII cranial nerve (facial nerve) prior or secondary to the condition was not excluded. The recommended investigations were blood-biochemistry tests, serological tests for Feline Immunodeficiency Virus (FIV) and Feline Leukaemia Virus (FeLV), abdominal ultrasonography and chest X-rays. It was also suggested that the nature of the lesions be investigated more thoroughly with diagnostic imaging (orbital ultrasound, computed tomography [CT] or magnetic resonance imaging [MRI] of the skull), and that further neurological and dental assessments be performed.

**Therapy**

Pending a definitive diagnosis the patient was given systemic antibiotic therapy (a combination of amoxicillin with clavulanic acid [Synulox®; Pfizer Italy, Latina, Italy: 12.5 mg/kg orally BID] and marbofloxacin [Marboey; Vetoquinol Italy, Bertinoro, Italy: 2 mg/kg per os SID]), which was preferred to other fluoroquinolones in cats because of its greater manageability at therapeutic doses and a local broad-spectrum antimicrobial agent (tobramycin eye drops QID: Stilbiotic; Ceva Vetem, Agrate Brianza, Italy) already in possession of the owner, together with topical administration of eye lubricants (polyacrylic acid QID: Lacrinorm® eye gel; Oftagen, Pisa, Italy).

**Diagnostic investigations**

A complete blood count showed a slightly increased haematocrit (47%; reference values 27.7-46.8%), while serum biochemistry showed increased levels of blood triglycerides (176 mg/dL; reference values: 35-95 mg/dL) and alanine aminotransferase (263 IU/L; reference values: 10-50 IU/L). Creatine phosphokinase and aspartate aminotransferase were slightly raised (191 IU/L; reference values: 40-180 IU/L and 48 IU/L; reference values: 10-40 IU/L, respectively). All other values were within the reference ranges. Serological tests with enzyme-linked immunosorbent assays (ELISA) for FIV and FeLV gave negative results.

Abdominal ultrasound and chest radiographs were normal and showed no signs suggestive of primary or metastatic neoplastic diseases. Contemporaneously, an ultrasonar examination of the retrobulbar space was performed, which showed modest, widespread hypochogenicity of right orbital tissues compared to those on the left.

The neurological assessment showed, in addition to the aforementioned neuro-ophthalmological lesions, in-
intermittent right circling and absent visual positioning on the right side. It was, therefore, decided to carry out diagnostic MRI in order to evaluate the brain and retrobulbar lesion simultaneously. The MRI study (VetRM, Esaote, Genoa, Italy) of the skull was performed using T1- and T2-weighted sagittal, transverse, and dorsal scans with short T1 inversion recovery (STIR) and fluid attenuated inversion recovery (FLAIR) gradient echo sequences, before and after injection of paramagnetic contrast medium (gadopentetate dimeglumine salt 0.2 mL/kg, Magnivist, Bayer, UK). These imaging studies revealed a lesion with clear margins that was hyperintense in the T2-weighted images and hypointense in the T1-weighted images and FLAIR sequences. The lesion, which involved the left parietal-temporal-occipital lobes and was confluent with the ipsilateral ventricle, was compatible with a porencephalic cavity as a sequela of the previous head injury described in the history (differential diagnoses: hypoxic-ischaemic injury, exposure to toxins, trauma, infection)\(^1\). There was also modest thickening of peribulbar soft tissues and the extraocular muscles on the right, which took up the contrast medium uniformly and appeared hyperintense on STIR sequences, as did the soft tissues surrounding the

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**Figure 1** - MRI study, transverse scans. T1-weighted images of the patient’s globes and orbits before (a) and after (b) administration of the contrast agent. The scleral and episcleral tissues of the OD appear thickened and the signal from fatty tissue is attenuated in the right orbit compared to that of the contralateral orbit (a, b). In the contrast-enhanced image, the homogeneous uptake of the contrast agent by the pathological tissues can be appreciated (b).

**Figure 2** - MRI study, dorsal scans. (a) STIR-weighted images: the right globe appears compressed and there is evident hyperintensity of the right scleral, episcleral and orbital tissues compared to the contralateral tissues. (b) Images acquired with the FLAIR technique: decrease in adipose tissue in the right orbit compared to the left.
roots of the premolar and molar teeth of the right maxilla (Figures 1 and 2). The differential diagnosis was between an inflammatory-infectious process or an infiltrative neoplastic process. It was, therefore, suggested that samples be taken for cytological and histological examination, a proposal that was declined at the time by the owner.

The dental examination revealed the presence of diffuse gingivitis, and exploration with a periodontal probe between the distal root of the right upper fourth premolar and the root of the right upper first molar showed a vertical loss of bone (3 mm by probing), due to grade II periodontitis, which was confirmed by intraoral radiographs (Figure 3).

**Evolution**

In view of the widespread nature of the orbital lesion and the clinical presentation, the diagnostic suspicion was FROMS and exenteration of the right orbit was recommended, but initially rejected by the owner. Following deterioration of the corneal lesion and the patient’s obvious discomfort the owner decided to consent to the operation which was performed approximately 4 weeks after presentation at the first visit (Figure 4). After premedication with methadone hydrochloride (Eptadone; Molteni Farmaceutici, Scandicci, Italy: 0.2 mg/kg) and dexmedetomidine hydrochloride (Dexdomitor®; Zoetis Italy, Rome, Italy: 0.002 mg/kg) administered intramuscularly, peripheral access was ensured with the introduction of a 22G catheter into the cephalic vein and anaesthesia was induced with intravenous propofol (Propofur; Merial, Milan, Italy: 4.5 mg/kg). The larynx was prepared with a lidocaine splash (Edocain Spray®; Molteni Dental, Milan, Italy) before intubating the patient with a 4.5 mm endotracheal tube. Anaesthesia was maintained with a mixture of 100% oxygen and isoflurane (Isoflo®; Esteve, Milan, Italy).

After shaving and cleaning the surgical field, the right orbital exenteration was performed using the standard technique with a transpalpebral approach, completely removing the upper and lower eyelids. The skin was closed with horizontal U interrupted absorbable sutures (polyglactin 910, Vicryl®; Ethicon Inc., Johnson & Johnson Medical, Pomezia, Italy). A combination of amoxicillin and clavulanic acid was administered postoperatively (12.5 mg/kg SID subcutaneously for 7 days). Post-operative recovery proceeded without complications. Histological examination of the ocular tissues, the globe and the orbital soft tissues (skeletal muscle and fibroadipose tissue) showed infiltration by proliferating spindle cells arranged in irregularly interlaced bundles. The cells had poorly distinct borders, a high nuclear/cytoplasmic ratio, eosinophilic cytoplasm, oval nuclei with finely dispersed granular chromatin and not evident nucleoli. Mitotic figures were rare. Multifocal lymphocytic aggregates were present within the neoplasia. The globe showed extensive corneal ulceration with secondary keratitis and neovascularisation as well as hypopyon. The histological diagnosis of a neoplastic lesion confirmed the clinical suspicion of FROMS.

At the follow-up control performed about 1 month after surgery, a small, elliptical area of the surface of the left cornea was noted: the area appeared dry and its central portion stained positively with fluorescein (Figure 5). OS blinking movements were present but incomplete. It was decided not to re-evaluate the animal’s mouth while it was not anaesthetised because of the cat’s decreasing collaboration. Following rapid deterioration of ocular conditions, about 5 weeks after the first operation, the owner agreed to exenteration of the left orbit, which was carried out with the procedure described previously. A new exploration of the oral cavity, performed during anaesthesia, showed bilateral gingivitis with areas of proliferative tissue at the level of the caudal parts of the left maxilla (Figure 6). No complications occurred.
during surgery and the post-operative recovery was also uneventful. The patient was given the same antibiotic therapy as that after the first intervention. Histological examination of the orbital tissues and left eyeball revealed the presence, in the orbital tissues, of a tumour with the same characteristics as those described for the contralateral orbit (Figure 7). The neoplastic cells showed moderate atypia with rare binuclear cells and from 0 to 1 mitoses per field (magnification 400X). A lymphocytic inflammation within the tumour was also noted in this case. In addition, there were signs of interstitial fibrosis of orbital muscles. The eyeball showed a corneal ulcer with neutrophilic keratitis, oedema and stromal neovascularization and multifocal lymphocytic episcleritis. The tumour was histologically compatible with FROMS.

At a follow-up carried out about 6 months after the second operation the patient was in a good clinical condition except for moderate drooling and feeding difficulties as a result of the increased size of the oral lesions (Figure 8). Recurrent tumours were not evident from palpation of the orbits. Advanced imaging studies were proposed to the owner for control purposes, but were rejected.

Following the rapid expansion of the patient's oral lesions and given the animal's inability to eat and drink, 1.5 months after the last follow-up, the owner chose to euthanise the animal, communicating this decision to the authors by telephone.

**DISCUSSION**

The first case of feline orbital pseudotumour, later reclassified as FROMS\(^3\), was described by Miller et al.\(^5\) in 2000. The term pseudotumour is commonly used to define masses of idiopathic origin histologically characterised by fibrosis and the presence of inflammatory cells of various nature without signs of infection or malignancy, although the prognosis, also in human medicine, can be unpredictable. Two cases of orbital pseudotumour, whose appearance and evolution were similar to those in humans, have been described in dogs\(^13,14\). In the feline case reported by Miller, the tumour, despite its similarity from a histopathological point of view to human orbital pseudotumour, had a very aggressive
clinical behaviour (contralateral extension) leading to the suspicion of a relationship with underlying systemic diseases (infectious diseases, endocrine diseases, autoimmune disorders, primary fibrosing disorders, drug reactions). A subsequent publication1, which included two cases of feline orbital pseudotumour, described the same fibroblastic appearance with inflammatory infiltrate and confirmed the clearly malignant clinical evolution.

In 2006, Billson et al.2, who re-examined seven cats with restricted eye movements, used the term “sclerosing orbital pseudotumour” on the basis of affinities with human “idiopathic sclerosing orbital pseudotumour” (ISOP). Similar pathological features were identified in all the cases analysed and the tumour was described as a primary fibrosis. Six patients presented with or developed contralateral involvement and, in all these patients, the owners opted for euthanasia. Three patients had also shown oral involvement. No condition described as a risk factor for the development of pseudotumour in human medicine was identified in this series of feline cases.

The inadequacy of the term pseudotumour was highlighted in 2011 by Bell et al.3 in a review of 12 cases archived in the Comparative Ocular Pathology Laboratory of Wisconsin (COLOW), including the case described by Miller et al.5 in 2000. In the light of the particularly aggressive biological behaviour of the tumour and the poor prognosis of affected individuals, the authors proposed the use of the term “feline restrictive orbital myofibroblastic sarcoma” while recognising the difficulties of interpreting biopsy specimens.

In the light of the particularly aggressive biological behaviour of the tumour, the term “feline restrictive orbital myofibroblastic sarcoma” was proposed.

The most recent case, published in 2013 by Thomasy et al.4, stressed the importance of reclassifying this disease from ISOP to FROMS on the basis of the prognosis and immunohistochemical characteristics. FROMS is a unique neoplasm of the adult/elderly cat (affecting animals from 7 to 17 years of age) with an often subtle onset but malignant clinical course. Interestingly, pseudotumours in cats show a different biological behaviour from that, essentially benign, of pseudotumours in other species, including dogs13,14,15,16,17,18. Other publications confirm this tendency. In a case presented by Volopich et al.19, with a biopsy diagnosis of orbital pseudotumour, the mass subsequently evolved into fibrosarcoma, while in a case of cutaneous pseudotumour secondary to a mycobacterial infection, described by Miller et al.20, the microscopic features were compatible with a spindle cell tumour rather than a granuloma.

The clinical case described here presented all the histological characteristics described in other cases of FROMS. The tumour cell population consisted of spindle cells arranged in long, irregularly interlaced bundles immersed in a variable amount of an extracellular eosinophilic substance (collagen) and infiltrated the orbital spaces and invaded adjacent structures. Anisocytosis and cellular anisokaryosis were mild or moderate and mitotic figures were rare. A lymphoplasmacytic-type inflammatory component is often present but not the dominant feature, in confirmation of the non-inflammatory nature of FROMS, and is concentrated predominantly in perivascular regions, as confirmed by the histological sections examined in the case reported here. There was extensive tumour infiltration in both specimens examined and it was not possible to identify histologically an area of the orbit with a higher concentration of neoplastic tissue. Likewise, in the previously described cases, this tumour had not shown a tendency to develop in particular areas of the periorbital space although the neoplastic tissue often appeared more

Figure 6 - Frontal view (a) and detail of the oral cavity (b) pre-operatively. There is an area of exposure keratitis with oedema and corneal neovascularisation of the OS and proliferative lesions of the maxillary gingiva can be seen.
abundant in the anterior and superior episclera, conjunctival substantia propria, and subcutis dermis and hypodermis of eyelids⁵. Any biopsies should, therefore, preferentially take specimens from these areas in an attempt to get diagnostic tissue⁵. Surrounding structures, such as the maxilla, hard palate, gums and nasal cavity may be variably involved while orbital fat and muscles only appear to be compressed. In the second specimen from the case we describe here, some orbital cartilage could be seen to be trapped by neoplastic growth and there was moderate interstitial fibrosis of parts of the orbital skeletal muscles, which also appeared compressed. New, advanced imaging studies or a full histopathological examination of the skull would have been able to show any involvement of surrounding structures but were declined by the owner. Immunohistochemical studies in FROMS show strong immunoreactivity mainly for vimentin and, variably, for α smooth muscle actin (αSMA) and S-100 protein⁶. Immunohistochemical studies are intended to characterise the origin of the lesion which also has a characteristic microscopic appearance. Histological samples from patients with FROMS also occasionally show changes attributable to secondary corneal lesions (e.g., ulceration, oedema, neovascularisation) and iridocyclitis (e.g., presence of inflammatory cells in the anterior chamber and at the level of ciliary processes)⁷,⁸,⁹.

The clinical case of FROMS described in this report confirms the difficulties in the diagnosis of this tumour. Indeed, although it is a real neoplastic disease, it has features of a syndrome with a range of symptoms that must be evaluated individually to avoid misinterpretation. FROMS is a neoplasm of cats with a clinical presentation characterised by exophthalmos, reduced movements of the palpebrae and globe, corneal lesions secondary to exposure and a tendency to extend to the contralateral orbit and adjacent structures, in particular the oral cavity. Exophthalmos and limited eyeball movements, recognised in the case reported here already at the initial clinical presentation, have been described in almost all cases published¹,²,³,⁴,⁵. The variable presence of these symptoms can be attributed to the spread of the tumour at the time of the examination or possibly to its starting site; in fact, in FROMS, a true mass is only established over time¹ and the starting site can be variable, even in the anterior orbit¹⁵. Exophthalmos can occur in companion animals with inflammatory diseases such as abscesses and cellulitis, with tumours (primary or secondary) and, more rarely, in cases of cystic disease (e.g., zygomatic mucocoele), developmental defects and trauma²²,²³. Orbital tumours are relatively common in cats and are the most frequent disease of the retrobulbar area in companion animals in general²¹. A case of exophthalmos secondary to an eosinophilic infiltration has been described in a feline²⁴. In humans, a correlation between eosinophil degranulation and local development of fibrosis has been suggested¹ but in no case of FROMS described in the literature, including the one presented here, has the presence of eosinophils been shown in histological sections or a significant increase been found in circulating eosinophils². Further studies in this direction are, however, justified. Exophthalmos due to space-occupying lesions is characterised by resistance to retropulsion of the globe and...
may be accompanied not only by corneal complications, but also by pain on palpation and opening the mouth. Ophthalmoscopy can be of help because there may be an indentation of the fundus, particularly in cases of retrobulbar neoplasm. In the clinical case described here, an area of indentation of the globe, never previously described in a case of FROMS, was present. The absence of other reports of this finding in the literature is probably due to corneal opacification, which can prevent evaluation of the fundus. Histological samples may also show compression and distortion of the globe which, together with a decrease in local blood flow, can also be responsible for retinal detachment.

Diagnostic imaging, particularly MRI and CT, can be of great help in cases of exophthalmos. Ultrasound examination of the oral cavity has shown some hypechoegenicity of orbital tissues and, rarely, a real mass effect. In the clinical case presented here, however, there was a degree of hypechoegenicity of signals from the orbital tissues. These findings confirm the limitations of ultrasonography as a method for visualising and characterising orbital tumours. In contrast, advanced imaging techniques (CT and MRI) have been shown to be able to detect typical anatomical features of FROMS, such as the thickening of the sclera and episclera, increased density of retro-orbital tissues, uptake of contrast medium, destruction of adjacent bony structures, thickening of the gingiva, hard palate and of the peri-ocular skin and invasion of the nasal cavities. The findings of the MRI examination in our case of FROMS were similar to those in the study by Thomsy et al.; moderate thickening of the peri- and retroorbital soft tissues without signal alterations in T1- and T2-weighted images, but hypointensity in the STIR sequences and T1 images following administration of the contrast agent. In our patient, advanced imaging also served to define the cerebral lesions (left porencephalus of probable traumatic origin) underlying the absence of the menace response OD and the patient’s psychomotor crises.

Keratitis is the most frequent reason for an ophthalmological examination in the case of FROMS. Keratitis may range from ulceration to corneal bullae. When corneal injuries are secondary to a blinking defect, as in this condition, the presence of both mechanical restrictions and neurological deficits must be assessed. In FROMS the exposure keratitis always has a mechanical component, with eyelid movements limited by the exophthalmos and palpebral infiltration, but a neurological component is also possible, due to entrapment of orbital nerve fibres and axonal degeneration. In the clinical case reported here, the altered appearance of the cornea was the first abnormality highlighted by the owner; furthermore, despite treatment, the particularly rapid progression of the corneal lesions led the owner to consent to orbital exenteration a few weeks after the onset of the first symptoms.

One of the most dramatic and characteristic aspects of FROMS is the bilateral orbital involvement as evidenced by all publications and in particular by two retrospective studies. In the study by Billson et al., six of the seven patients presented with or developed the condition in the contralateral orbit within a period ranging from 6 weeks to 7 months. In the clinical cases studied by Bell...
et al.\(^2\) the period ranged from 4 to 8 months\(^3\). It is, however, interesting to note that in this latter study, five out of the 12 patients had unilateral disease, in four of which cases the orbital tumour was present in combination with oral involvement. To date the longest latency period prior to the detection of contralateral involvement is approximately 1.5 years\(^6\). In all cases with bilateral orbital involvement the owners finally opted for euthanasia\(^1,2,3,4,5,6\) even though the animals' general clinical conditions were overall good. In the clinical case described here the time between the initial presentation and the appearance of the first clinical signs of contralateral orbital involvement (surface keratitis and impaired blinking) was approximately 8 weeks. There is, therefore, great variability in the rate of spread of FROMS to contralateral tissues and it is difficult to predict the speed of its progression. Involvement of the oral cavity has been described in almost all studies on FROMS, and is often already detectable at the initial presentation\(^1,2,3\), which can make the diagnosis even more complex by causing clinical pictures overlapping with those of dental conditions. Given the open structure of the orbit in companion animals, with the retro-orbital space being separated from the oral cavity by only soft tissues (zygomatic gland, pterygoid muscle and orbital fat), it is relatively frequent that diseases of these areas spread to the other. Maxillary and pterygoid muscle and orbital fat), it is relatively frequent that diseases of these areas spread to the other. Maxillary dental diseases may be responsible for orbital inflammatory problems, while retrobulbar space-occupying lesions can spread and invade the oral cavity or cause secondary destruction of adjacent bone structures\(^2,27\). The odontostomatological alterations in FROMS vary from generalised gingivitis\(^4\) to gingival hyperplasia\(^5\), and a certain degree of thickening of the gingiva and soft palate can also be appreciated by advanced diagnostic imaging\(^6\). Histologically, the oral lesions are neoplastic infiltrations of the lamina propria and palate\(^1\). In those cases in which the tumour spreads to the oral cavity, this expansion became clinically evident in a period from 3 to 14 months\(^5,14\) after the ophthalmological symptoms. Gingival proliferations can make it difficult for an animal to feed, thus driving the owners to choose the euthanasia\(^1\).

This study describes for the first time the radiological appearance of the dental arches of a cat with FROMS from an early stage of the oral involvement. The patient's dental examination did not detect proliferative lesions or specific bone alterations at the time of the initial ophthalmological presentation, whereas the MRI study of the soft tissues surrounding the roots below the affected orbit showed alterations compatible with both an inflammatory process and a neoplastic one. At a subsequent clinical exploration of the oral cavity (less than 2 months after the first ophthalmological examination) newly formed gingival tissue was unequivocally present. These observations show that the spread of FROMS can be unpredictable and very fast, and also demonstrate that the clinical presence of buccal lesions may be helpful but is not essential for making the diagnosis. Importantly, in this clinical case, advanced imaging provided the indication to take targeted biopsy samples, which would have been useful for establishing the diagnosis and making a prognosis, but were refused by the animal's owner.

Given the possible secondary origin of orbital pseudotumours in humans, attempts have been made to identify diseases underlying this tumour also in feline species.

In human medicine, herpes zoster may be associated with some forms of orbital myositis\(^28\) but all attempts to isolate or identify Feline herpesvirus (FHV-1) in cytological\(^2\) or biopsy samples\(^2,4\) from cats with FROMS have so far failed. Further tests occasionally performed to evaluate the positivity of subjects for other viral infections (FIV, FeLV, Coronavirus)\(^1,2\) have also so far excluded that such agents have a role in the pathogenesis of FROMS.

In corroboration, serological tests for FIV and FeLV in the case reported here were also negative. Nevertheless, future studies are recommended to definitively rule out a possible correlation between these infections in cats and FROMS.

One of the main differential diagnoses in cases of fibrosclerosing orbital diseases in humans is thyroid orbitopathy in which autoimmune-based endocrine disorders are responsible for inflammation, swelling and fibrosis of the retrobulbar tissues, mainly involving extraocular muscles\(^29\). Although some animals with FROMS have shown thyroid abnormalities (an increase in T4 in one case\(^2\), and post-mortem findings of thyroid adenoma and thyroiditis in another case\(^6\)) no unequivocal link between these diseases has been detected in cats, also in the light of the different histopathological presentation\(^5\). The presence of foreign bodies and previous trauma can also cause inflammatory orbital disease and local formation of granuloma\(^20\) in humans and animals\(^21\). Particular attention must be paid to this pathogenesis in cats, given the long-recognised relationship between traumatic events or the presence of foreign bodies and the development of sarcomas\(^28,29\). Nevertheless, the past histo-
All the therapeutic efforts taken to counter the progression of FROMS have had disappointing results. Systemic treatments with antibiotics\(^2\),\(^3\), anti-inflammatory steroids\(^1\),\(^2\),\(^3\) and immunosuppressants\(^1\),\(^4\), individually or in combination, have been tried but without obvious success. Likewise, antiviral therapy has not resulted in benefits for treated patients\(^3\),\(^4\),\(^32\). Local treatment with antibiotics and lubricants can give relief but cannot be considered curative, as confirmed by the clinical case described here. In some cases, temporary tarsorrhaphy or operations to correct entropion have been carried out to preserve corneal integrity but these surgical approaches are also only palliative\(^2\),\(^4\),\(^5\). Not even the use of radiotherapy has provided substantial improvements\(^1\),\(^2\) except in one case in which it was suggested to have reduced clinical symptoms\(^6\). The results of further studies in this direction are awaited. To date the only therapeutic approach recommended for FROMS is early orbital exenteration which, although it has not been demonstrated to be definitely effective in stopping the spread of this cancer, can potentially delay its progression\(^6\) and provide some improvement in the clinical condition of affected individuals.

CONCLUSIONS
FROMS is a relatively rare spindle cell cancer that is unique in the feline species. This cancer typically involves the orbital tissues causing symptoms similar to those of other retrobulbar space-occupying lesions (resistance to retropulsion, severe decrease in eyelid mobility, exposure-induced corneal disorders), although with fast progression and an aggressive course. Despite a histopathological appearance comparable to that of pseudotumour in other animal species, FROMS shows a malignant clinical behaviour, with frequent bilateral extension and spread to adjacent tissues. Although metastases to other organs have never been identified, the prognosis for patients with this tumour is often poor, culminating in euthanasia for animals unable to feed because of oral involvement. FROMS has shown little response to the medical therapies attempted so far and the recommended therapeutic approach remains surgery with complete orbital exenteration even though this does not guarantee that the growth of the tumour will be arrested. The case presented here confirms the knowledge about FROMS acquired to date and describes the oral extension of this cancer. Since aggressive, early surgery can potentially improve a patient’s prognosis, the importance of a prompt, accurate clinical diagnosis is clear. The distinction between FROMS and other orbital tumours relies on the clinical features, diagnostic imaging and histopathology. In the case of suspected FROMS, the biopsy sampling for histological studies should be carried out precisely, preferentially from the anterior and superior episclera, the conjunctival substantia propria, the hypodermis and the deep dermis of the palpebrae\(^3\).

ACKNOWLEDGEMENTS
We thank Prof. Massimo Mariscoli, Prof. Maria Teresa Mandara, Dr. Chiara Giudici, Dr. Valentina Andreani, Dr. Ilaria Pitzorno, Dr. Luigi Settimi, and Dr. Annalisa Piomponi for their cooperation and the material they provided.

KEY POINTS
- FROMS is characterised histologically by the presence of spindle cells with a low mitotic index arranged in irregular bundles and moderate collagen deposition. This tumour tends to infiltrate along the fascial planes surrounding orbital tissues, causing their compression.
- The oral cavity is involved in almost all cases of FROMS, often already at the first presentation, and evolution in this site may be the main reason for euthanasia of affected patients.
- FROMS has shown a poor response to treatment.
REFERENCES


