

## Histopathology and treatment of nine cats with multiple epulides

### *Histopathologie en behandeling van negen katten met multipele epulides*

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#### ABSTRACT

**In this article 9 cases of Multiple Feline Epulides (MFE) are discussed. All cats presented with multiple gingival masses covering most of the teeth. Eight cases were diagnosed as reactive hyperplasia and one was a as peripheral ossifying fibroma. Eight were Domestic Shorthair cats and one a Domestic Longhair. No sex predilection was found. All cats were young at first presentation. In 8 of the cases, cure was achieved by gingivoplasty and extraction of all premolars and molars and sometimes the incisors. In the 1 case that was treated more conservatively, without extractions, multiple recurrences were seen.**

**The results of the present study are compared to findings in previously published reports on multiple epulides in cats.**

#### SAMENVATTING

In dit artikel worden 9 gevallen van feliene multipele epulides besproken. Alle katten werden aangeboden met multipele gingivale massa's die het merendeel van de tandkronen bedekten. Acht gevallen werden gediagnosticeerd als reactieve hyperplasie en 1 als perifeer ossificerend fibroma. Acht katten waren Europese Kortharen en 1 was een Europese Langhaar. Geslachtsprevalentie werd niet gezien. Alle katten waren jong op het moment dat de epulides voor het eerst werden opgemerkt. In 8 gevallen bleken gingivoplastie en de extractie van alle kiezen en soms snijtanden curatief. Een geval werd meer conservatief behandeld, zonder extracties. Bij deze kat recidiveerden de epulides.

De resultaten van deze studie worden vergeleken met de bevindingen uit de literatuur.

#### INTRODUCTION

An epulis is a nonspecific gingival growth. It is a clinically descriptive term used for tumors and tumor-like masses of the gingiva (Carranza, 2002; Verstraete *et al.*, 1992). An epulis can be benign or malignant, and can be reactive or neoplastic (Gorrel, 2004).

Verstraete *et al.* (1992) and Verhaert (2005) both reported in non-related studies that one out of five epulides in dogs were malignant neoplastic lesions. Verstraete (1992) reported 43.5% focal fibrous hyperplasia, 17.5% peripheral ameloblastoma, 16.9% peripheral odontogenic fibroma, 1.95% pyogenic granuloma, and 1.95% other odontogenic tumors. Verhaert (2005) reported 63 reactive lesions, one ‘fibromatosis’ and 36 neoplastic epulides (twenty of which were locally aggressive or malignant) in a series of 100 epulides. Malignant gingival enlargements that are found are predominantly squamous cell carcinoma, malignant melanoma or fibrosarcoma.

Epulides can be single or multiple. In this article only the Multiple Feline Epulides (MFE) will be discussed.

MFE is a rare condition in cats. In the recent literature only a few reports on multiple epulides in cats exist. Colgin *et al.* (2001) reported 13 cases of MFE, Gracis *et al.* (2001) reported three cases and De Bruijn *et al.* (2007) reported 11 cases of MFE in a series of 52 cases of epulides in cats. Gingival hyperplasia presenting as protuberant masses resembling neoplasms are a well recognized condition in Boxers and other, usually large breed dogs (Harvey and Emily, 1993), and are considered reactive rather than neoplastic lesions.

MFE is reported to occur in cats ranging from one to 15 years of age (Colgin *et al.*, 2001; Gracis *et al.*, 2001; De Bruijn *et al.*, 2007). In 50% of all reported cases, the cats were 3 years or younger. The clinical signs include multiple sessile, irregular, often inflamed gingival masses covering most of the crowns of the af-

ected teeth (Gracis *et al.*, 2001). MFE does not affect the cat's general health much.

A lot of confusion exists about the true nature and biological behavior of this type of epulides. Colgin *et al.* (2001) concluded that MFE should be considered to be fibromatous epulides of periodontal ligament origin, an odontogenic lesion. Gracis *et al.* (2001) concludes that these cases are benign neoplasms, i.e. peripheral odontogenic fibroma or fibromatous epulis. In the report by De Bruijn *et al.* (2007), the term fibromatous epulis is again used for MFE. Gardner (1982, 2002) examined several samples of MFE and considered them to be equivalent to the peripheral ossifying fibroma, a reactive lesion in humans that arises from the periosteum.

The treatment option recommended by Colgin *et al.* (2001) is wide excision of these growths to avoid recurrence. Gardner (2002) recommended a more conservative excision, concentrating on the removal of any irritants.

De Bruijn *et al.* (2007) reported that 4 out of the total of 6 recurrences within the 2 year follow-up period after marginal excision of single or multiple epulides occurred in the cases of multiple epulides.

Gracis *et al.* (2001) reported that cure was achieved in all cases after dental extractions, alveoloplasty and gingivectomy.

This article presents nine cases of MFE in cats, outlining treatment, histopathology and outcomes.

## MATERIALS AND METHODS

During the period of 2001-2008 seven patients with Multiple Feline Epulides (MFE) were referred to the authors for examination. The patients were presented for obvious proliferations at the gingival margin, with or without oral malodor, and with no other clinical problems. All cats were being fed both dry and canned food at the time of presentation.

All patients were premedicated with ketamine and medetomidine (Domitor<sup>®</sup>). They were intubated and anesthesia was maintained with oxygen and isoflurane (Isoflo<sup>®</sup>). Further analgesic treatment consisted of buprenorphine (Temgesic<sup>®</sup>) intraoperatively and a NSAID (meloxicam, Metacam<sup>®</sup>) postoperatively. Anesthesia was monitored in all cases with a capnograph and an ECG or pulsoxymetry. Full-mouth preoperative radiographs were taken.

The initial treatment that was performed in most cats was professional periodontal treatment (scaling and polishing) and removal of the MFE with a number eleven scalpel blade and a sharp curette (gingivoplasty). Hemostasis was obtained in all cases by light pressure with gauze swabs, without the use of cauterization. NSAID's were given for a short period (3 to 5 days). No antibiotics were prescribed. The owners were advised to perform dental homecare on a daily basis by brushing the teeth, with or without the use of a dental diet (Hills feline t/d<sup>®</sup>), after healing of the gingiva.

After a period of 6 weeks to 3 months, treatment

outcome was evaluated. If the lesions recurred, dental extractions and alveoloplasty were performed on one or both sides after removal of the MFE by gingivoplasty. If teeth were only extracted on one side, gingivoplasty was performed on the opposite side and the remaining teeth scaled and polished. The reason for extracting teeth on one side only was to evaluate outcome of gingivoplasty and extractions versus gingivoplasty only in the same animal. No antibiotics were prescribed, and only NSAID's were given for a short time.

In the third treatment, the remaining premolars and molars were removed and alveoloplasty and gingivoplasty were performed in those cats that still had any premolars and/or molars left.

An additional two patients were treated by a general practitioner, who removed the MFE and sent the samples to the first author.

All MFE samples were sent to the Department of Oral Pathology, Faculty of Odontology, Malmö University (Sweden) for histopathological examination.

The specimens were fixed in ten percent formalin before they were sent to the laboratory. In the laboratory they were dehydrated, embedded in paraffin and sectioned into three  $\mu\text{m}$  thick sections. Sections were stained with hematoxylin-eosin and viewed under a light microscope fitted with a digital camera (Olympus DP12<sup>®</sup>).

## RESULTS

The MFE presented as multiple sessile, irregular, inflamed gingival masses covering most of the crowns of the affected teeth. Examples are shown in Figures 1 and 2. The edentulous sites were normal. Eight patients were European Domestic Shorthair cats (DSH) and one was a Domestic Longhair cat (DLH).

The age of the cats ranged from 8 months to 14 years. The oldest cat (case number 4) showed MFE since the age of 2. Five of the cats were neutered males and 4 were neutered females. All the patient details are organized in Table 1.

The general physical examination of the cats was unremarkable. The cats appeared in good body condition. Oral examination was performed under general anesthesia and, apart from MFE, the only abnormalities found in these cases were plaque and some calculus deposits on most teeth. One cat had a fractured right maxillary canine tooth. Full mouth radiographs showed no abnormalities other than soft tissue swellings.

All the cats had a recurrence of MFE within a period of 6 weeks to 3 months after professional periodontal treatment and gingivoplasty. In 3 cases the owner was able to perform dental homecare, but despite homecare, the lesions recurred. In case 1, at the 6 weeks post-op re-examination the epulides were much more pronounced on the right side as compared to the left side. Interestingly enough, the owner reported that brushing was technically easier on the left side.



**Figure 1. Clinical presentation of case no.1, European Shorthair cat, female (neutered), 1 year old with MFE.**



**Figure 2. Clinical presentation of case no.3, European Shorthair cat, male (neutered), 2 ½ years old, with a close-up photo of MFE.**

Recurrence was seen at tooth-bearing areas only after gingivoplasty. No recurrence was seen at previous extraction sites, except in case number 3. Eight months postoperatively, this cat presented with MFE around the incisors and at some previous extraction sites of premolars. Dental radiographs showed no root tips or dental material left at the extraction sites. The MFE were removed using a number 11 scalpel blade, and no recurrence was seen after that. An example of the long-term result after gingivoplasty and extraction is shown in Figure 3.

Case number 5, presented to a general practitioner, was treated in the same manner as the author’s series and exhibited the same features: recurrence after gingivoplasty and cure after multiple extractions.

Case number 4, seen by a general practitioner, was presented with a history of MFE since the age of 2. MFE were removed by thermocautery on a yearly basis up to the age of 14, after which the owner declined further treatment. At that age the cat was euthanized.

The histopathology of all samples showed hyperplastic gingiva with moderate inflammation. The location of the epulides and the histopathological results are presented in Table 2.

In 6 cases, the stroma was fibroblast rich, highly



**Figure 3. Clinical presentation of case no. 1, two months after extraction of premolars and molars. No recurrence of MFE was seen after treatment.**

vascularized and covered by inflammatory reactive epithelium without dysplasia.

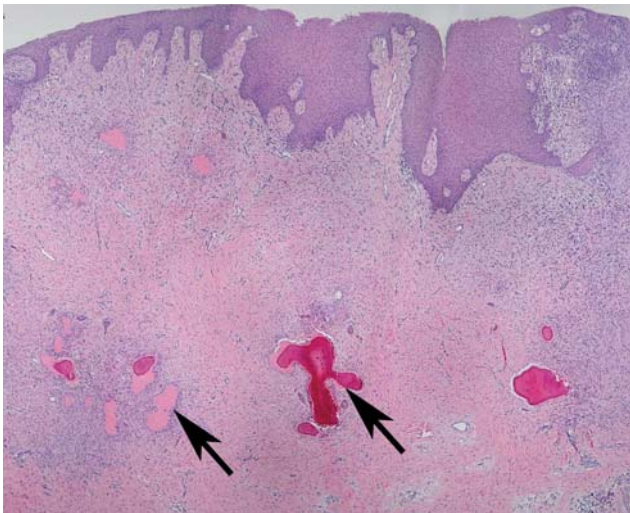
Cases 1 and 5 showed a comparable histopathology of hyperplasia, though these cases involved more fibrous but still rather fibroblastic areas containing small hard tissue fragments. The histopathological presenta-

**Table 1. Case summaries of patients with MFE.**

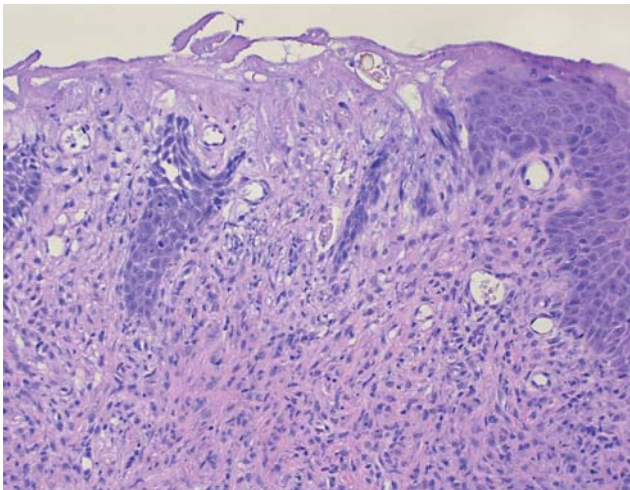
Case	Age of first presentation	Sex	Breed	Treatment	Recurrence	
					After gingivoplasty	After dental extractions
1	1 year	FS	DSH	staged	Yes	No
2	8 months	MN	DSH	single		No
3	2 ½ years	MN	DSH	staged	Yes	Yes
4	2 years	MN	DSH	staged	Yes	No extractions
5	3 years	FS	DSH	staged	Yes	No
6	8 months	FS	DSH	staged	Yes	No
7	2 years	MN	DSH	single		No
8	2 ½ years	FS	DSH	single		No
9	1 ½ years	MN	DLH	staged	Yes	No

(FS: female spayed; MN: male neutered; DSH: Domestic Shorthair; DLH: Domestic Longhair)

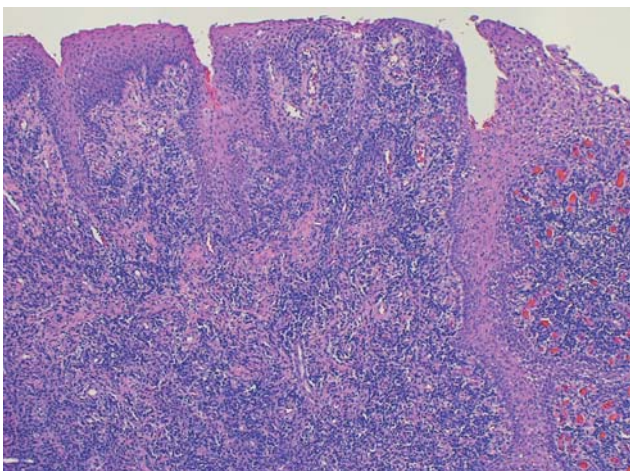




**Figure 4. Case no. 5 (10x):** small islands of partly calcified bone/cementum (arrows) in a fibrous stroma with varying degrees of cellularity (hematoxylin-eosin stained).



**Figure 5. Case no.5 (20x):** high magnification shows a growth with cellular and richly vascularized stroma. The surface is ulcerated with features of previous mechanical trauma (hematoxylin-eosin stained).



**Figure 6. Case no.7 (hematoxylin-eosin stained):** a more traditional inflammatory hyperplasia with strong inflammation rather than the fibroblast rich and less inflamed stroma seen in the multiple lesions of the other cases.

tion of case number 5 is shown in Figures 4 (10x magnification) and 5 (20x magnification).

Case 7 showed more of a traditional inflammatory hyperplasia with strong inflammation rather than the fibroblast rich and less inflamed stroma seen in the multiple lesions of the other cats (Figure 6).

The samples of the recurrent MFE in case 3 showed hyperplastic gingiva with fibroblast rich stroma, which in some areas was also rather collagen rich with small fragments of metaplastic hard tissue.

All of the samples were considered reactive and not convincingly neoplastic. All but case one were designated as 'reactive hyperplasia', with small hard tissue fragments in case 5 and the recurrent epulides in case 3. Case 1 was diagnosed as peripheral ossifying fibroma.

## DISCUSSION

MFE is a rare condition in the cat. In the article by Colgin *et al.* (2001), there are 13 cases of MFE in cats between 1 and 15 years of age (mean age 5.3 years). In the case report by Gracis *et al.* (2001), 2 cats were 6 years old and one was 8 years old. In the article by de Bruijn *et al.* (2007), there are 11 cases of MFE in cats between 1 and 14 years of age (mean age 4.4 years). By way of summary, half of the cases in these 3 reports taken together are in cats 3 years old or younger. In the study presented here, the ages of all the cats were between 8 months and 14 years at the time of presentation, but all of these cats showed the first signs at a young age (3 years or younger). It can be concluded that MFE is a disease with a high prevalence in young cats.

In the studies by Colgin *et al.* (2001), Gracis *et al.* (2001) and de Bruijn *et al.* (2007), there was no sex predilection for MFE and the most commonly reported breed was the Domestic Shorthair. In the present study, 5 of the cats were male and 4 female. All the cats were neutered. The breeds represented included 8 European Domestic Shorthair cats and 1 Domestic Longhair cat. Unlike with dogs, there seems to be no breed predilection in cats. The most commonly reported breed in the dog is the Boxer, in which an inherited cause is suspected (Harvey *et al.*, 1993).

The multiple epulides in the present study were located consistently around the premolars and molars in the mandible and/or maxilla, and in some cases also around the incisors and/or canine teeth. In the study by Colgin *et al.* (2001), there is no report of size and location of the gingival masses. Gracis *et al.* (2001) reported multiple sessile, irregular, inflamed, friable masses covering most of the crown height. In only 1 case were the carnassial teeth affected. In the study by de Bruijn *et al.* (2007), the size and location vary, but most lesions were found around premolars.

In the present study, for all but one of the cases the histopathological diagnosis was reactive hyperplasia. In 1 case, the diagnosis was peripheral ossifying fibroma, which is also a reactive lesion and not a neoplasm (Cawson *et al.* 2001, Neville *et al.* 2002). This is in

**Table 2. Localization and histopathological diagnosis of the epulides.**

Case number	Localization	Histopathological diagnosis
1	Incisors, premolars, molars	Peripheral ossifying fibroma
2	Premolars, molars	Reactive hyperplasia
3	Maxillary incisors, premolars, molars, mandibular molars	Reactive hyperplasia
3 (recurrence)	Incisors, right mandible	Reactive hyperplasia (with hard tissue fragments)
4	Incisors, premolars, molars	Reactive hyperplasia
5	Unknown	Reactive hyperplasia (with hard tissue fragments)
6	Premolars, molars	Reactive hyperplasia
7	Premolars, molars	Reactive hyperplasia
8	Mandibular third premolars and maxillary fourth premolars	Reactive hyperplasia
9	Incisors, lower canines, premolars and molars	Reactive hyperplasia

contrast to the conclusions of Gracis (2001), Colgin *et al.* (2001) and de Bruijn *et al.* (2007) in their reports.

Gracis *et al.* (2001) classified the 3 cases as peripheral odontogenic fibroma, an odontogenic tumor. All the cases in the study by Colgin *et al.* (2001) were fibromatous epulides, which were considered neoplastic lesions by the authors. In the study by de Bruijn *et al.* (2007), most of the epulides showed a combination of lesions. The most frequently diagnosed lesion was the “fibromatous epulis” with a combination of acanthomatous and ossifying components.

Although the lesions in the present report resemble histologically what was designated as “fibromatous epulis” in the studies by Colgin *et al.* (2001) and de Bruijn *et al.* (2007), the authors of the present report consider them to be reactive lesions, as opposed to the view of Colgin *et al.* (2001), who considered them to be neoplastic lesions. None of the samples show strands of odontogenic epithelium, a hallmark of peripheral odontogenic fibroma (Gardner, 1982, 2002), while they do show all the features of gingival hyperplasia. Therefore, they should not be classified as the true ‘fibromatous epulis of periodontal origin’, or peripheral odontogenic fibroma, but rather as ‘hyperplasia’ and ‘peripheral ossifying fibroma’. Binnie (1999) differentiates peripheral ossifying fibroma (a reactive lesion) from peripheral odontogenic fibroma (a benign neoplasm) by the abundance of strands and islands of odontogenic epithelium in the peripheral odontogenic fibroma. Peripheral ossifying fibroma is generally considered to be a reactive lesion in response to irritations such as plaque and calculus, and is not related to central ossifying fibroma, which is a neoplasm of bone (Cawson *et al.* 2001, Neville *et al.* 2002). In humans, it occurs exclusively on the gingiva, predominantly in young adults, and usually presents as a single lesion. Women are affected more often than men and there is a predilection for the anterior part of the jaws (Neville *et al.*, 2002). Peripheral ossifying fibroma is characterized by a fibrous proliferation in which bone- or cementum-like hard tissue is formed (Holmstrup *et al.* 2003).

Gingival hyperplasia is a common feature of gingival disease in some dog breeds, as for example Boxers (Harvey, 1993; Gorrel, 2004), and also in hu-

mans (Carranza, 2002b). According to Carranza *et al.* (2002b), the accepted current terminology for this condition is gingival enlargement or gingival overgrowth.

Inflammatory gingival enlargement (Carranza *et al.* 2002b) can be caused either by an acute or a chronic disease. Both a chronic and an acute inflammation produce changes in the normal firm and resilient consistency of the gingiva. The first step is infiltration by fluid and cells of inflammatory exudate. There is a phase of marked softness and friability, followed by a phase of firm leathery consistency (Caranza *et al.* 2002a). This is due to fibrosis and epithelial proliferation associated with long-standing chronic inflammation. Chronic inflammatory gingival enlargement is caused by prolonged exposure to dental plaque (Carranza *et al.*, 2002b).

Besides inflammatory gingival enlargement, other causes of gingival enlargement are well recognized. Drug-induced gingival enlargement has been described and is a well known consequence of the administration of some anticonvulsants (e.g. phenytoin), immunosuppressants (e.g. cyclosporine (Nam *et al.* (2008)) and calcium channel blockers (e.g. verapamil, amlodipine (Thomason *et al.* 2009)). The clinical and microscopic features of the enlargements caused by different drugs are similar (Caranza *et al.* 2002b).

Enlargements in humans can be associated with systemic conditions such as pregnancy, puberty, vitamin C deficiency, leukemia and granulomatous diseases (Carranza *et al.*, 2002b).

None of the cats in the current study had received medication prior to the development of MFE, all had been neutered, and none of them showed signs of systemic disease. Therefore, it is unlikely that any of these secondary factors could have influenced the occurrence of MFE. Plaque-induced inflammatory enlargement seems to be the most likely cause in this series of cats.

Initial treatment of the MFE in this study, which consisted of removal of the growths either by means of a scalpel blade or by means of a thermocauter, was not successful. In all cases, there was recurrence of the MFE. Colgin *et al.* (2001) reported recurrence in eight out of the thirteen cases after marginal excision, and therefore advises wide excision. Gardner (1982, 2002)



recommends a more conservative approach, with marginal excision while concentrating on removal of irritants to the gingiva. One cat of the Colgin *et al.* (2001) series was euthanized after recurrence, which seems unnecessary since none of the reported cats had generalized health problems. In the study by de Bruijn *et al.* (2007), four out of the total of 6 recurrences of epulides occurred in multiple epulides within the two-year follow-up period after marginal excision.

Only after extraction of the premolars, the molars and in some cases also the incisors was the excision of the epulides successful in the series presented. This is in accordance with the findings in the case report by Gracis *et al.* (2001), where cure was achieved in all cases after dental extractions, alveoloplasty and gingivoplasty. In humans, as well, both gingival hyperplasia and peripheral ossifying fibroma have a tendency to recur after surgical excision, so an attempt should be made to remove any irritants (such as plaque) at the time of surgery (Gardner 2002, Neville *et al.*, 2002).

Interestingly, in one cat that received daily tooth brushing, recurrence was more obvious on the side of the oral cavity that, according to the owners, was technically more difficult to brush. It therefore seems that at least in this case plaque was a contributing factor for the development of MFE.

In summary, the MFE cases in this study were all reactive lesions, and none of the samples were considered to be neoplastic. One case of peripheral ossifying fibroma was diagnosed, and all the others were reactive hyperplasia. The age of first presentation of the MFE in the cats was between 8 months and 3 years. None of the cats had dental resorptive lesions or any other irritating factor other than plaque and some calculus in the oral cavity that could explain the generalized gingival enlargements or MFE. None of the cats was under medication with any of the substances known to cause gingival enlargement. Hormonal factors were not present, since all the cats were neutered. In the authors' opinion, MFE is most likely caused by an irritating factor such as dental plaque at the gingival margin in susceptible animals. Successful treatment of MFE seems to be largely dependent on the removal of these irritants. Extraction of all teeth showing MFE takes away the plaque retentive surfaces, and therefore adequately removes all plaque in the long-term from that location. Therefore, the most successful outcome in the long term can be expected after multiple dental extractions, alveoloplasty and gingivoplasty.

#### ACKNOWLEDGEMENTS

Dr.G. Warfvinge and Dr. A. Larsson, Department of Oral Pathology, Faculty of Odontology, Malmö University Sweden for the histopathological evaluation of our samples.

Mrs.P. Kindermans (DVM) and Mr. S. Heslinga (DVM), for sharing clinical findings and sending MFE samples of cases 4 and 5 to the authors.

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