

# Treatment of a case of refractory feline chronic gingivostomatitis with feline recombinant interferon omega

**Chronic gingivostomatitis is a common debilitating disease in cats, which is often refractory to medical and surgical treatment. An eight-year-old, neutered female domestic shorthair cat with a history of gingivitis was presented with chronic gingivostomatitis. Initial treatment by extraction of all premolars and molars was unsuccessful. However, the condition resolved within six weeks of treatment with feline recombinant interferon omega (Virbagen; Virbac).**

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*Journal of Small Animal Practice* (2006)  
DOI: 10.1111/j.1748-5827.2006.00166.x

## INTRODUCTION

Feline chronic gingivostomatitis (FCGS) is a common condition of the cat characterised by intense inflammation of gingival and non-gingival oral mucosa. Clinically, lesions are described according to the location within the oral cavity (Hennet 1997). The two specific sites affected are the glossopalatine mucosa (palatoglossitis or "faucitis") and the buccal mucosa overlying the premolar/molar arches (buccostomatitis). Affected cats may show mild to severe dysphagia, with slight to absolute reluctance to eat. The decline in food intake leads to progressive apathy and weight loss.

FCGS is often refractory to medical treatment (Harley and others 1999), with no treatment regimen demonstrating superiority (Harley and others 2003). The extraction of all premolar and molar teeth has given the most dependable results with up to 80 per cent of cats being clinically cured or significantly improved (Hennet 1997).

It has been suggested that there is an immune-mediated component to FCGS, although the mechanism for this is uncertain (Harley and others 1999). Histologically, the inflammatory infiltrate typically contains plasma cells, lymphocytes, macrophages and neutrophils.

Various infective agents have been implicated in the development of FCGS including feline calicivirus (FCV), feline immunodeficiency virus (FIV), feline

leukaemia virus (FeLV) (Hennet 1997) and various bacteria including *Porphyromonas* (Mihaljevic 2002).

Interferons are cytokines that have antiviral, antiproliferative and immunomodulatory effects (Tompkins 1999, Bauvois and Wietzerbin 2002) through direct and indirect effects on target cells. Studies have shown that treatment with feline omega interferon (FeIFN) increases the survival time of cats infected with FeLV and/or FIV (De Mari and others 2004), clinically improves cats with herpetic keratitis when applied topically (Verneuil 2004) and shortens the duration of acute calicivirosis in experimentally infected cats (Yoshizumi and others 1993, Mochizuki and others 1994, Belin 2002). It may thus also be effective in treating cats with FCGS in which infection with FCV is a contributory factor.

## CASE REPORT

An eight-year-old, neutered female domestic shorthair cat was presented in January 2003 with severe chronic gingivostomatitis.

The cat had a history of gingivitis dating back to March 2002. It had received periodontal therapy, consisting of supra and subgingival scaling using an ultrasonic scaler and crown polishing using a prophylaxis cup and pumice paste in a slow-speed handpiece, in March and again in May 2002. The cat tested negative for FeLV and FIV using an in-house test kit (Witness FeLV/FIV; Merial) in May 2002.

On presentation in January 2003, the cat had severe inflammation of the buccal and glossopalatine mucosa. It again tested negative for FeLV and FIV. An oropharyngeal swab taken from the glossopalatine mucosa for FCV isolation was positive. A series of full-mouth radiographs (10 views) were taken before tooth extraction. These were unremarkable. All teeth except the canines were extracted using a surgical technique. Postoperative management consisted of a single intramuscular injection of 1.5 mg morphine,

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50 mg amoxicillin/clavulanate tablets (Synulox; Pfizer) twice daily and flushing the oral cavity with 0.12 per cent chlorhexidine gluconate daily for five days.

In March 2003, the cat was re-presented with unresolved chronic gingivostomatitis (Fig 1). There was severe inflammation of the oral mucosa and glossopalatine folds. Oropharyngeal swabs were taken for FCV isolation and feline herpes virus (FHV) polymerase chain reaction (PCR). Blood was taken for FeLV isolation and FIV PCR. Of these tests, only the FCV isolation was positive.

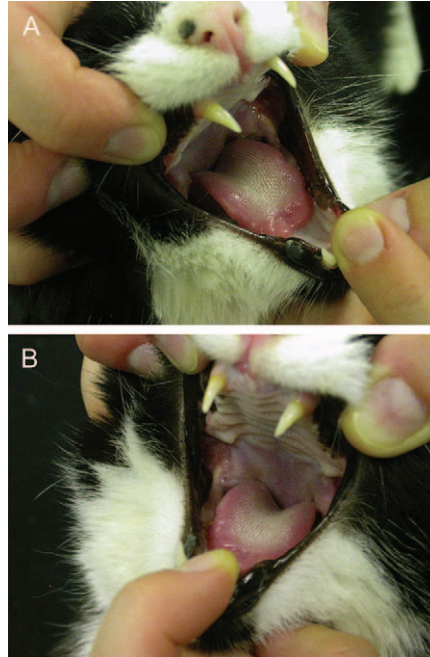
Treatment was started with 1 mega unit/kg recombinant FeIFN given by subcutaneous injection on alternate days for five doses. After the fifth dose, 10,000 iu FeIFN in 2 ml of isotonic saline was given orally by the owner once daily for two months and then on alternate days for the third month. No other medication was given.

The cat was re-examined, and oral swabs were taken for FCV isolation after six (Fig 2a,b), 10 (Fig 3) and 14 weeks.

There was a significant reduction in oral inflammation, and no FCV was isolated. Six months later, the cat was re-examined under general anaesthesia. There was very slight inflammation of the glossopalatine folds (Fig 4). Swabs were taken from the tonsils and tonsillar crypts for FCV PCR. The result was negative.

## DISCUSSION

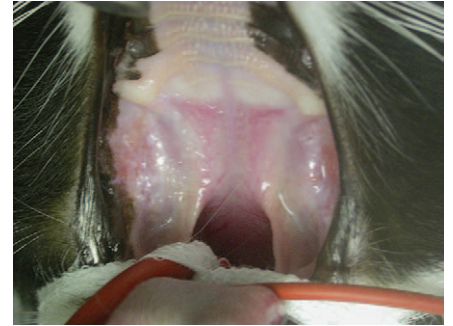
The role of FCV in the development of FCGS is unclear. FCV has been isolated from up to 100 per cent of FCGS cases



**FIG 2A,B.** Much reduced oral inflammation six weeks after starting treatment with feline omega interferon

compared with up to 25 per cent of cats in a healthy population (Coutts and others 1994), indicating that the carrier state may be a pre-requisite for the induction of chronic stomatitis (Knowles and others 1991, Hennet and Boucraut-Baralon 2003). However, FCV isolated from cats with FCGS and then inoculated into specific pathogen free cats produced signs of acute calicivirosis but not FCGS, suggesting that other factors contribute towards the development of the oral inflammation.

Clinical cases of FCGS are not related to distinct FCV biotypes (Poulet and



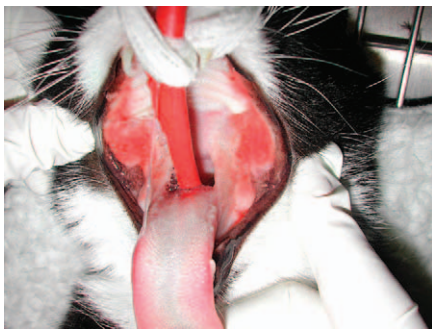
**FIG 4.** The initial improvement has been maintained. This picture was taken six months after treatment with feline omega interferon

others 2000), but the chronic carrier state is characterised by the emergence of antigenically distant viruses. It is postulated that the rapid genetic and antigenic change seen in FCV may lead to immune escape and the development of persistent infections. This would suggest that development of FCGS is more likely associated with the host immune response to chronic FCV infection rather than the development of particularly pathogenic distinct FCV strains.

Cats with FCGS have been shown to have raised serum concentrations of immunoglobulin (Ig) G, IgM and IgA and raised salivary concentrations of IgG and IgM but significantly lower concentrations of IgA (Harley and others 2003). IgA neutralises pathogens and toxins in the oral cavity, inhibits the adherence or growth of microorganisms on the oral mucosa or teeth and enhances non-specific defence factors. It is unclear whether the Ig pattern described is a cause or a result of the inflammatory disease.

Histological examination of tissue from persistently infected cats indicates that FCV replicated only in epithelial cells of the superficial tonsillar epithelium or adjacent fossa mucosa (Dick and others 1989).

Localisation occurs in the tonsils in the acute phase of FCV infection, possibly as a consequence of their function as a filter. The degree of tissue damage and viral invasion is insufficient to induce significant inflammation (Dick and others 1989). Most carriers are asymptomatic. It is possible that, in cats with some form of immune deficiency, the balance of this carrier state is affected and increase in virus



**FIG 1.** Oral inflammation two months after multiple tooth extraction but immediately before treatment with feline omega interferon



**FIG 3.** Normal oral mucosa with no evidence of inflammation 10 weeks after treatment with feline omega interferon

replication and invasion stimulates a more severe immune response. The most common reported clinical sign associated with FIV is gingivostomatitis (Tenorio and others 1990, Williams and Aller 1992), supporting the supposition that immune deficiency is an important factor in the development of FCGS.

This case demonstrated a clear relationship between initiation of treatment with FeIFN, cessation of shedding of FCV and resolution of FCGS. This supports the view that FCV is an important factor in the development of FCGS (Addie and others 2003). However, the fact that FCGS often resolves in FCV-positive cats after the extraction of all teeth and the consequent reduction in dental plaque suggests that other antigenic stimuli are involved in the pathogenesis of the disease.

As far as the authors are aware, this is the first case where the FCV status of a cat has been monitored before, during and after treatment with FeIFN and that FCV shedding ceased rapidly after the initiation of treatment.

It is unclear whether the cessation of shedding is related to immunomodulatory or antiviral effects of FeIFN. One hypothesis is that, through its immunomodulatory effect, FeIFN reduces the inflammation associated with FCGS which eliminates the chronically inflamed tissue that FCV requires to replicate. This, however, ignores the fact that most cats shedding FCV are asymptomatic, with little or no oral inflammation, suggesting that chronic inflammation is not a prerequisite for the FCV carrier state or viral shedding. Therefore, it remains possible that the antiviral effect of FeIFN is more significant.

FCGS resolves in many FCV-positive cats following full-mouth extractions without any specific antiviral treatment, supporting the hypothesis that a number of factors are involved in its development. Teeth provide the main surface for plaque accumulation in the oral cavity. Multiple

tooth extraction will therefore greatly reduce oral plaque levels. It is possible that it is the sum of the total antigenic stimulation from plaque bacteria and viruses that is significant for the development of FCGS.

Five other cases of FCGS (all of which were FCV positive, FeLV and FIV negative and had had surgical extraction of at least all premolar and molar teeth) have been treated with FeIFN in a similar way by the authors. FeIFN was given at 1 mega unit/kg by subcutaneous injection on alternate days for five doses, and this was repeated 30 days after the first injection. No oral FeIFN was given. Three of the five cases resolved. One cat improved but needed long-term management by flushing the oral cavity with 0.12 per cent chlorhexidine gluconate daily. The fifth case relapsed soon after the end of the treatment. Interestingly, this case has since completely resolved after a single treatment with intra-lesional injections of 5 mega units of FeIFN.

No adverse effects following administration of FeIFN were noted in any of the above cases.

FCGS is a common and debilitating condition in cats. Approximately 80 per cent of cases resolve with multiple tooth extraction. Treatment of the 20 per cent of non-responsive cases can be frustrating. The clinical improvement seen in the cases reported here would suggest that FeIFN therapy may be useful in cases that are refractory to surgical treatment.

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