Feline Chronic Gingivo-Stomatitis (FCGS)

Introduction

The condition currently, and most commonly, known as Feline Chronic Gingivo-Stomatitis (FCGS) is a relatively common and frustrating problem to the small animal practitioner. A number of synonyms are found in the literature for the same conditions. Examples are “Feline Lymphocytic Plasmacytic Stomatitis”, Plasma Cell Stomatitis”. The reported incidence varies with severity but a figure of 3% of all feline dental conditions for the most intractable cases may be considered reasonable. Many cases prove to be extremely frustrating with a number of different combination treatments in current use.

The syndrome is characterised by persistent and severe inflammation and ulceration of the oral, pharyngeal and lingual mucosa. The two specific sites are the mucosa lateral to the glossopalatine arches (palatoglossitis) and the mucosa overlying the cheek teeth, known as buccostomatitis. The condition is often present in the absence of significant accumulation of calculus on the teeth. It can develop initially around the time of kitten vaccination or temporary teeth eruption but also as permanent teeth erupt or, most commonly much later in life. Purebred cats have long been considered to be over-represented. There is also an inverse relationship between the age of onset of disease and the number of cats in the household and this may implicate social stress or increased exposure to infectious agents as predisposing factors.

This syndrome is best considered as part of a full oral cavity examination and the presence of Feline Tooth Resorption (TR’s) lesions frequently adds to and confuses the picture. It is not clear whether the gingival inflammation precedes, contributes to, or is a result of the TR’s. The syndrome appears to have a number of subsets of which those cats with Feline TR’s is only one. Additionally, there is some concern that it may be a pre-neoplastic lesion and also that calici virus infection is a co-factor in the induction or progression of the complex. Although the relationship between calici infection and FCGS appears strong, there is also a reported incidence of 50% of cats infected with FIV also having FCGS. Another source indicates that around 15% of cats with FCGS are positive for FeLV/FIV. (Knowles 1989)

One consistent feature of all cases is a hypergammaglobulinaemia. This implies B lymphocyte proliferation and therefore no humoral immune response depression. It is probable that affected cats are intolerant to even small quantities of bacterial plaque on the tooth surface and elsewhere in the mouth. The main problem is that not all FCGS cases are alike in that some respond to routine periodontal therapy and improved hygiene while others will respond poorly to treatment. The implication is that some cats have a very low threshold to the trigger factors(s) whilst others have a higher threshold approaching the level for normal cats. Most intractable cases (87%) improve with elective tooth extraction and a few cases (13%) do not respond to any treatment. (Hennet 1997, Girard & Hennet 2005)

Clinical Signs

The main sign in all cats is dysphagia and pain due to oral inflammation. Often this is more than would be expected with predictable dental disease. Inflammatory lesions can be focal or diffuse and may involve all oral tissues (gingiva, palatine, lingual or buccal mucosa and, possibly, the fauces). Lesions are more commonly found caudally towards the glossopalatine arches where saliva pools. It is common to see inflammation crossing the mucogingival line into the buccal or vestibular mucosa. This tends to be a bad prognostic indicator. For all affected tissues secondary ulceration and infection can occur.

Signs reported are:

- Ptyalism, dysphagia, halitosis.
- Weight loss - chronic or acute
- Lack of (or an inability) to groom.
- Cachexia - history may be acute but probably chronic. A reluctance to eat hard food is common.
- Submandibular lymphadenomegaly – often dramatically increased in size and painful when palpated.
- Variable accumulation of plaque and calculus.
- Teeth may be missing, affected by “neck lesions” or suffering from furcation exposure and excessive mobility after recession of the periodontal tissues.

Aetiology

There is no simple aetiological agent for this syndrome. Certain factors are known to have an effect but the most commonly held view is that these cats suffer from an immunological over-reaction to low levels of oral antigens – dental plaque mainly. Factors involved are:

1. Breed: Some breeds may appear to have more affected individuals. Purebred cats are *anecdotally* more often affected with Siamese, Burmese, Abyssinian, Persians, Tonkinese, and Main Coons all over represented.

2. Environmental Factors: Colony cats or those in multi-cat households appear to be more commonly affected. *Stress* is considered to be the main factor with also the close proximity of animals allowing transmission of microorganisms also being significant.

3. Plaque bacteria: The oral bacteria present in the plaque matrix drive the abnormal non-specific inflammatory response. Although individuals are thought to be plaque intolerant there is a variable threshold to the bacterial load among these individuals. Specific bacteria as seen in periodontal disease have been reported in these cats and Bartonella henselae has also been implicated, albeit controversially, in the USA.

4. Feline Viruses: Testing at Bristol Veterinary School and elsewhere indicated that up to 100% of chronically affected individuals (> 6months) show positive testing to oropharyngeal swabbing for Feline Calici Virus. In chronic cases the virus can persist in the tonsils and fauces. The significance of this in the syndrome is not known. It is possible that the virus damages cell membranes allowing easier antigenic penetration

by other agents. However, other co-factors are required before this virus can cause disease. One research study (Hennet & Boucrault-Baralon) considered that chronic palatoglossitis lesions, as opposed to buccostomatitis lesions, to be calicivirus associated.

Feline immunodeficiency virus (FIV), feline leukaemia virus (FeLV) and feline herpes virus (FHV) have also been implicated in the past. FIV particularly may have a role in producing oral lesions by predisposing the cat to secondary infections. Both FIV and FeLV may contribute to an aberrant immune response to oral antigens.

5. Dental Disease: The presence of concurrent dental disease is important. Either periodontal disease or Feline Tooth Resorption lesions (FTR's) or both can have an exacerbating effect on the syndrome.

Pathogenesis

Microscopically, mild mucosal lesions are characterised by epithelial hyperplasia accompanied by a mixed mononuclear inflammatory cell infiltrate dominated by plasma cells and lymphocytes. As the lesions become more severe there is epithelial degeneration and ulceration accompanied by immigration of neutrophils, resulting in a mixed chronic-active inflammatory cell infiltrate. In these mature lesions the proportion of plasma cells, lymphocytes, macrophages and neutrophils will vary depending upon the degree of epithelial degeneration and secondary infection, although plasma cells and lymphocytes still usually predominate.

Serum IgG, IgM and IgA levels are raised in cats with chronic gingivostomatitis, although the mechanism underlying this polyclonal response is not understood. Furthermore, cats with chronic gingivostomatitis have increased salivary IgG and IgM concentrations, but decreased salivary IgA levels. It is not apparent if the relative deficiency in salivary IgA is due to inherent factors, or is a consequence of the disease. Nevertheless, the low levels of IgA within the saliva of cats with chronic gingivostomatitis may contribute to the development and/or persistence of the condition by reducing the effectiveness of the local oral defence mechanisms. Furthermore, increased concentrations of salivary IgG and IgM might have a detrimental effect on the oral tissues by provoking increased inflammation through the activation of complement.

Clinical Investigation

A standard clinical approach is advocated for all cats affected. This should comprise:

- Virus testing for FIV, FeLV. Oral swab for FCV.

- Routine Haematology and Biochemistry screening for underlying systemic disease. One study (Hennet 1997) reported 10% of affected cats with chronic renal failure. Any underlying systemic disease may significantly affect the prognosis or the safety of anaesthetic protocols.

- Biopsy of affected areas - necessary mainly to eliminate malignant neoplasms (e.g. Sq. Cell Carcinoma) and other immunopathologies.

- Radiographic full mouth dental survey to assess status of teeth, bone quality and locate broken root tips or Feline TR's.

Treatment

There are basically three underlying principles to treatment regimes.

- **Control plaque**
- **Control existing dental disease – periodontal disease and tooth resorptive lesions mainly**
- **Control inflammation**

All affected individuals should be treated in basically the same manner given that the ultimate aim is to improve the overall hygiene of the oral cavity and reduce the antigen burden by, initially a thorough dental scaling, periodontal debridement and polishing followed by aggressive home care with 0.12% chlorhexidine gluconate gel twice daily. (Parodongyl™: Virbac).The main aim is zero tolerance of both existing dental disease and of bacterial plaque.

Base-line Treatment - all cases

Antibiotics - often necessary pre-operatively to control excessive inflammation and improve quality of soft tissue before and after surgery.
Metronidazole at 10mg/kg bid, Doxicycline (Ronaxan: Merial) at 0.2mg/kg bid, Antirobe: Pfizer) at 11mg/kg sid, Spiramycin/Metronidazole (Stomorgyl: Merial) at one Stomorgyl 2 per 2kg sid and Amoxycillin/clavulanate (Synulox: Pfizer) at 12.5mg/kg bid
Use pre-op as required to improve tissues and post-op for minimum 8-10 days. Ensure owner can comply with treatment. This may mean using an antibiotic in acceptable form. Metronidazole and Clindamycin can be hidden in frozen butter balls or pilchards with tomato sauce.

Dental Surgery Perform full and diligent scale with Slimline ultrasonic tip to eliminate all calculus and necrotic cementum from supra and subgingival areas.
Special attention must be paid to pockets with the use of a small subgingival curettage. Extract teeth not viable. Polish as normal with a prophy cup.

Homecare - This is an essential part of the treatment and should be considered a vital and on-going part of a successful regime. Failure to comply with homecare will lead to an inevitable failure of the treatment as a whole. Compliance is the key to success to reduce antigen burden. First choice should be a chlorhexidine containing agent (Paradongyl Gel: Virbac) as it is effective against the major pathogens implicated here – including viruses. Administration should be twice daily, preferably gently, via a small cat brush (Virbac) or a baby toothbrush with soft bristles.

Additional Treatment - Selected Cases

Gingivectomy

Necessary in cases where hyperplastic gingiva has created a pseudo-pocket deeper than the normal sulcus depth the body can deal with through the normal immune mechanisms. In cats, this depth can be as small as 0.5mm. Best performed with scalpel and a bevelled cut 120º to the long axis of the tooth. An electrosurgery machine on cut/coagulation mode using a wire loop can also be used as can a small rugby ball shaped diamond bur in a high speed handpiece. This latter method requires extreme care not to damage tooth surface. For both the loop and the diamond bur it is still necessary to "scallop" the gingiva at the inter-dental area. Remember that up to 1mm may slough at the margin of an electrosurgery incision.

Repeat Scale / Polish

For juvenile patients it is important to avoid permanent anatomic changes in the first two years of life. If the immune system is substandard in the early days of life, the provision of excellent hygiene can help considerably. Although little calculus may be visible, continued inflammatory changes in either the whole of the gingiva or the marginal gingiva is an indication to repeat the surgical cleaning - especially the hand curettage subgingivally.

Elective Tooth Extraction

Any teeth that exhibit dental resorptive lesions (FTR's) must be removed using a technique suitable to their type (i.e. Type 1 or Type 2). In addition, once periodontal recession has created pocketing and exposure of the furcation angle, the provision of dental home-care to maintain a quiescent state will be very difficult. In these circumstances, extraction of the tooth/teeth is a wise choice.

However, it is often necessary to remove multiple cheek teeth in this condition. In the authors opinion if the tissues fail to respond to the best hygiene you can provide within 2-4 weeks by reduction of inflammation and improvement in comfort, the best option is elective surgical extraction of all the cheek teeth. Owners and many veterinary surgeons are often reluctant to take this step. The prognosis for this procedure can broadly be estimated that 50% of all cases will resolve without further need for treatment, 37% will improve but will require less medication than before but varying degrees of continuing anti-inflammatory treatment and 13% will not improve (Girard, 2005).

Elective surgical extraction of whole cheek teeth quadrants should not be undertaken lightly as there are several problems associated with it.

1) The underlying bone may be sclerotic and poorly vascularised.
2) The roots may be ankylosed to the alveolar bone
3) Teeth affected by Tooth Resorption lesions (type 2) may have roots in an advanced state of destruction with no true morphology. For type 1 TR lesions the teeth may be fragile and hard to extract without flaps.

Best results will be achieved by surgical extraction. Flush oral cavity and sulcus area with 0.12% chlorhexidine gluconate (Hexarinse™: Virbac) and scale teeth pre-extraction to minimise the amount of debris in the mouth.
Use a # 11 scalpel blade to break down the epithelial attachment round each tooth with a sulcar incision. For whole quadrant extractions, make one releasing incision in the mucus membrane caudal and one mesial (rostral) to the target teeth block on only the buccal surfaces. Strip back the soft tissues full thickness with a small periosteal elevator to reveal the teeth and the bone. With a high-speed bur (Round # 1) and water irrigation, remove a small

amount of crestal bone around each tooth to expose the buccal root surfaces and the furcation angle. Once the furcation is exposed, multi-rooted teeth can be split into single roots in an apical to coronal direction. A small channel created with a size half or one round bur will assist the luxation of the root. A sharp root tip pick or a small dental elevator is used carefully in an apical and axial direction along the long axis of the root and round its circumference to loosen the root within the alveolus. Once loose, and not before, the root can be rotated out of its socket with small extraction forceps.

Dental Luxators for Cats

- Feline Luxator – 301 serrated (EX5S)
- Feline Luxator – 301 (EX5)
- Feline Luxator – 301 modified (EX5H)
- Feline Slimline Luxator (100C)

Sources: kruuse.uk@kruuse.com or www.dunlops.com or www.drshipp.com

In a very few circumstances it may be desirable to resort to crown amputation and intentional root retention ***only*** if Type 2 FORL's are present. The exposed bone should be flushed copiously with isotonic saline and smoothed before closure of the mucosal flaps. This can be performed with a bone rasp or a high speed diamond bur. Suture the gingiva using an absorbable material with a swaged-on cutting needle. (5/0 Monocryl with PS2 needle)

Multiple extraction's require consideration as to analgesics, antibiotics and nutrition post-op. Buprenorphine (Vetergesic™: Alstoe) is considered good for moderate to severe pain in cats at 1ml per 15kg every 6 hours. This can be used either parenterally or per os/sublingual. Owners can administer this analgesic very easily. An alternative regime would be to use a selective μ-agonist opioid such as morphine. Morphine is very useful for severe pain at 0.1mg to 0.2mg/kg im or sc. every 6-8hrs. One analgesic modality that is receiving more attention by veterinary dentists is the use of local or regional blocks in addition to systemic administration. The advantages are augmentation of the traditional analgesics and reduction of the inhaled anaesthetic agent by a reported 0.5 to 1% of Mean Alveolar Concentration. NSAID's also have a place with due attention to the possibility of underlying renal or hepatic problems. Carprofen or meloxicam have been used successfully.

Antibiotics and analgesics should preferably be started pre-operatively. The selected drug should have good activity in bone and on anaerobic bacteria. Soft foods are necessary for three to five days post-op. In extreme circumstances it may be necessary to use a convalescence diet immediately post-op such as Hill's a/d™, Waltham Feline Concentration Diet™ or Nutrigel™ (Virbac).

Other Anti-inflammatory or Immunomodulation Therapies

1. Antibiotic therapy

Antibiotic therapy can be used either long term or in pulse form but, following elective extraction of cheek teeth, has minimal beneficial effect in many cases. There are reports of the use of a low dose Doxicycline regime (Preshaw 2004). Dose quoted is 0.2mg/kg bid although other sources quote as high as 2mg/kg bid. The low dose is submicrobial and is used long term between professional cleaning. It has anti-collagenase properties at this dose and has not been shown to cause antibiotic resistance. Metronidazole has also proved useful at a dose of 10mg/kg bid. This drug is not easy to give in cats. The tablet can be powdered and placed in butterballs and given frozen or paediatric syrup can be used with an acceptable flavour.

2. Interferon

A number of veterinary surgeons report using Interferon but, at this time, there are still few published long-term studies to indicate whether it exceeds the potential of any other treatments for this condition. However, literature has started to appear indicating the circumstances in which it is likely to help.

A double blind study has been running in France to assess the effects of Interferon in a group of FCV positive cats that have proved non-responsive to elective dental extractions. Publication is expected in 2008.

Preliminary results indicate the Interferon may be most effectively used in the group of cats, which are FCV positive and are non-responders to extraction. This conclusion has been confirmed in a single case study (Southerden P 2007).

Subgingival or submucosal use: A single treatment total dose of 5 MU injected locally into the junction between healthy gum and diseased tissues provides a strong antiviral effect. Given post-surgery when the cat is anaesthetised, this method has been reported by two authors to have excellent results (Camy 2004, Mihaljevic 2004). Initially, using a 10MU vial, half the volume is drawn into an insulin syringe. Draw enough saline or sterile water into the syringe to provide a reasonable volume for use. The contents can be administered in fractions of 0.1ml. The remaining 5MU from the vial can be injected into a 100ml saline bag as described below in “Oral Use” paragraph.

Improvement in visible inflammation may take up to three months. In the meantime an immunomodulatory dose of 50,000 units of interferon can be given daily by the owner per os – see below.

Oral use: Interferon given per os is believed to work by initiating a cytokine cascade when it comes into contact with cells. The cascade then has distant effects. This regimen of administration best follows a single dose of 5MU injected submucosally as described in the previous paragraph. A 5MU dose is initially diluted into a 100ml bag of sterile saline and fractions of 10ml created which are frozen. When frozen they have a reported shelf life of one year. The first 10ml fraction is used to give a dose of 1ml per os per cat per day. This fraction can be refrigerated normally and will have a shelf life of three weeks. The owner continues to give 1ml per day until all the fractions are used. Ideally, treatment lasts for six to eight week but longer may be required. After three months, the treatment should be reassessed.

Subcutaneous injections: This method of administration is described but appears to be less effective than submucosal administration for oral carriage of FCV. One regime described is 1 mega unit/kg once every other day for five treatments. Thereafter attempt to reduce dosage to twice a week provided the cat is still doing well. Discontinue treatment only after three attempts to isolate calicivirus have been negative (these can be at weekly intervals). A reported alternative is to follow an oral regime at home after the five injected treatments.

Monitoring the cat's weight is a useful objective way of assessing response to treatment. Note that feline interferon omega should always be stored in the fridge and will remain viable once reconstituted for up to 21 days at 4^{o}C. when used for low dose oral administration – not for injection.

3. Corticosteroids

In general, the use of corticosteroids is not recommended for cats which are virus positive for FeLV, FIV or FCV. They are used by some practitioners principally to control inflammation in a hyperimmune response in cats in which their use is not contraindicated. This is indicated by hypergammaglobulinaemia and/or plasma cell infiltrate in tissue. Some authors consider their use contraindicated totally.

They can be used per os, parentally or intralesional. One study has found methylprednisolone acetate (Depomedrone™: Pfizer Animal Health) to be the most effective form of corticoid short term. It can be injected at a dose of 2mg/kg up to 20mg (0.5ml) IM at intervals of 2-3 weeks for three to six treatments until a response is obtained then no more frequently that every 6 weeks. One can also use immunosuppressive doses of prednisolone at 1mg - 4mg/kg daily in divided doses initially but some sources report a less predictable control than using injectable depot corticoids. Dexamethasone at 0.1mg/kg/day has also been used in cases refractory to prednisolone. As a response is achieved, the doses can be reduced as far as possible with the aim of using the minimum effective dose.

Chlorambucil (Leukeran) has also been used for this condition and for eosinophilic granuloma in the mouths of cats. Reported doses are 2mg per cat once or twice a week.

Cyclosporine is an agent that has been extensively used with varying success rates although it is not licensed for cats. It mainly blocks T-helper cells but may also suppress T-suppresser cells and inhibit release of various lymphokines such as interleukin 2 and T cell growth factor. Doses in current use vary but 2mg/kg bid is used by many clinicians. Absorption is erratic but Neoral (Novartis) seems to get the best reported absorption. To that end, blood levels are checked 4-6 weeks later and adjusted as required to avoid toxicity and ensure that trough levels are maintained at adequate levels of 250-500ng/m. Over 750-1000 ng/m approaches toxic levels. Once the cat responds the dose can be reduced by lifetime use and monitoring is necessary for most. Known side effects are hepatic dysfunction, renal dysfunction and anaemia. Labs which perform this test are Antech (www.antechdiagnostics.com/index.htm) and Idexx (www.idexx.com/aboutidexx/locations).

Progestagens (megestrol acetate) have direct and indirect inflammatory effects but also severe undesirable side effects – principally diabetes mellitus, lethargy, and obesity. Doses used have been 2.5mg daily for one week then once weekly or 5mg for three days then 1.25mg twice weekly.

Laser Therapy

The use of CO_2 and other lasers has also been under investigation with no clear recommendations available as yet. Laser treatment has been used but to date no reliable data exists to commend their use on a regular basis. Anecdotal reports do indicate good responses in some cats. The main problem is the expense involved in purchase of the units. Another suggestion was the ***Dentron Biogun*** which kills micro organisms with a concentrated stream of electrically charged air particles which de-esterify the fatty acids on the phospholipid biolayer of the microbial cells causing lysis. Further information is available on www.dentron.co.uk

Food

Food may be an important feature in managing this condition. Some affected cats improve on a balanced, additive free food such as Butcher's Classic Cat Food. In addition, after dentistry, cats fed on Hills a/d diet gained more weight and had smaller lesions than those fed on a control diet (Theyse *et al*, 2003). Glasgow Veterinary School currently recommend a change to either of these foods for cats suffering from this condition.

Summary

The consensus at the present time is that this is a poorly defined syndrome of unknown aetiology characterised by focal or diffuse chronic inflammatory response involving the gingiva, oral mucosa, and often the pharyngeal fauces.

Commonly described clinical findings include elevated serum globulins and a submucosal infiltrate of plasma cells, lymphocytes, neutrophils, and macrophages. Potentially various viral agents and bacterial species are involved. There is no doubt that atypical immune responses are the basis of the problem. This complex can occur with either immune deficiencies or, more commonly, exaggerated immune responses and to that end multiple mechanisms will be acting concurrently.

Successful management of this complex requires a logical approach. The need for base-line data before treatment alters the host response cannot be over-stated. Once this data is available a treatment plan and prognosis can be considered. The role of bacterial plaque is crucial whatever the state of the host immune response. Diligent professional scaling, polishing and subgingival debridement - zero tolerance to any dental disease - underpins any treatment in tandem with aggressive homecare by the owner. Cases failing to respond to simple plaque control should be considered for elective cheek teeth extraction at an early date. Those cases still non-responsive but FCV positive may be helped by interferon therapy. It is important that the owner is involved at an early stage with discussions as to aetiology, treatment plans and help with homecare. A highly motivated owner is a strong ally in the provision of successful treatment.

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