

Feline Gingivostomatitis: What We Know and How We Treat It

Cindy Charlier, DVM, DAVDC
Fox Valley Veterinary Dentistry and Surgery
Chicago, IL

Stomatitis is a term used to describe widespread inflammation of the oral cavity. Gingivostomatitis means inflammation of the gingival tissues and oral cavity. Cats with stomatitis may have inflammation or ulceration and/or proliferative lesions anywhere within the oral cavity. The lesions may involve the gingival tissues, alveolar mucosal tissues, caudal buccal mucosal tissues, the area lateral to the palatoglossal folds in the caudal oral cavity, the sublingual tissue and/or the oropharyngeal tissues.

Terms used to describe oral and oropharyngeal inflammation in the feline oral cavity include:

- Gingivitis: inflammation of the gingiva
- Periodontitis: inflammation of the non-gingival periodontal tissues (periodontal ligament and alveolar bone)
- Alveolar mucositis: inflammation of the alveolar mucosa (mucosa overlying the alveolar process and extending from the mucogingival junction without obvious demarcation to the vestibular sulcus and floor of the mouth)
- Sublingual mucositis: inflammation of the mucosa on the floor of the mouth
- Labial / buccal mucositis: inflammation of the lip / cheek mucosa
- Caudal mucositis: inflammation of the mucosa of the caudal oral cavity, bordered medially by the palatoglossal folds and fauces, dorsally by the hard and soft palate and rostrally by the alveolar and buccal mucosa
- Palatitis: inflammation of the mucosa covering the hard and soft palate
- Glossitis: inflammation of the mucosa of the dorsal and/or ventral tongue surface
- Cheilitis: inflammation of the lip (including the mucocutaneous junction area and skin of the lip)
- Osteomyelitis: inflammation of the bone and bone marrow
- Stomatitis: inflammation of the mucous lining of any of the structures in the mouth; in clinical use the term should be reserved to describe widespread oral inflammation (beyond gingivitis and periodontitis) that may also extend into submucosal tissues (i.e. marked caudal mucositis extending into submucosal tissues may be termed caudal stomatitis).

Etiology/pathogenesis

It is thought that stomatitis is a multifactorial disease where the cat's immune system responds inappropriately to chronic oral antigenic stimulation of various origins. Antigens may include plaque bacteria, feline calicivirus and food proteins. Periodontal disease, tooth resorption, as well as viral infections (FIV, Feleuk, calici, herpes) have been suggested to play a role. Genetic predisposition, food allergies, and bacteria may also play a role in feline oropharyngeal inflammation. Current thought is that cats with feline chronic gingivostomatitis have an inappropriate response or 'hyper' immune response to the dental plaque bacteria. Specific bacteria, as seen in periodontal disease, have been reported in these cats. *Pasteurella* and *Prevotella* species are more highly represented than others. Calici virus is present in 97% of cats affected by chronic oropharyngeal inflammation when compared to a control group (25%); however no cause and effect has been established. Some cats with stomatitis test positive for *Bartonella*, but again a cause and effect has not been established. We do not know for sure what causes the disease which makes treatment of the disease challenging.

Cats with chronic gingivostomatitis most often have bilateral disease. Differential diagnoses include eosinophilic granuloma complex, periodontitis, neoplasia (squamous cell carcinoma, fibrosarcoma), uremic stomatitis, caustic chemical ingestion, plant irritation, electrical cord burn, food allergies, and systemic autoimmune diseases (lupus, pemphigus).

History and clinical signs

A thorough history is the first step in evaluation of any patient with oral disease. Factors to be considered include the patient's diet, age at onset of clinical signs, onset and duration of clinical signs, environmental hazards, chronic illness, and / or systemic disease. The median age of affected cats is seven years. No gender predilection has been reported.

Clinical signs may include anorexia, weight loss, hypersalivation, pawing at the face, pain when opening the mouth or yawning, dropping food, and/or reluctance to eat hard food. The patient's haircoat may be matted and unkempt due to the decrease in self grooming that occurs secondary to oral pain. Halitosis and blood tinged saliva may also be present.

The second step in patient evaluation is a complete physical exam to evaluate all organ systems. A complete intraoral examination will help to determine the extent of disease and identify any teeth with tooth resorption or periodontal disease. A complete examination under general anesthesia including full mouth radiographs is the only way to determine the true extent of oral pathology.

Laboratory tests should include a CBC, biochemistry profile, thyroid panel and urinalysis to rule out concurrent systemic disease. A feline leukemia and FIV test should be completed to rule out concurrent viral disease. Many cats with stomatitis will have elevation

of total protein and globulins. Other tests that may be included in the patient evaluation are toxoplasmosis titer, Bartonella screening, viral testing for calici and herpes virus, immune profiles (ANA) and serum protein electrophoresis.

Treatment

Feline stomatitis is often a frustrating disease to treat. As there is no known single etiology, treatment success varies with every case. The goal of treatment is to restore the balance between the cat's immune response and the oral antigen burden. Currently there is no known medical protocol that consistently has positive *long term* results. Treating with medications usually is only masking the underlying issue of a hyperimmune response to plaque. Extraction of teeth in the vicinity of the alveolar mucositis and caudal stomatitis and extracting teeth with periodontal disease or tooth resorption in order to suppress any chronic oral antigenic stimulation has shown the best results.

The extent of disease at the time of presentation determines the appropriate first stage of treatment. If the patient presents with *very mild* disease, initial treatment includes periodontal therapy, full mouth radiographs and extraction of any teeth affected by periodontal disease or tooth resorption. The goal of treatment is to remove the bacterial plaque and bacterial byproducts that are toxic to the periodontal tissues with thorough supragingival and subgingival scaling and polishing. It is imperative to remove all inflammation within the oral cavity. Biopsy of affected tissue should be obtained to rule out neoplasia. Histopathology of the mucosa and submucosa reveals dense infiltrates of plasma cells with lesser numbers of lymphocytes, neutrophils and macrophages which is consistent with virtually any inflammation in a cat's mouth. After the procedure, daily home care is required to maintain a plaque free environment. A chlorhexidine gel applied daily may assist with plaque control. Daily brushing, if the cat will allow it, remains the most effective way to control plaque. In addition to daily brushing, use of Veterinary Oral Health Council (VOHC) accepted diets, treats and/or water additives to control plaque is recommended.

If the owner is unable or unwilling to provide homecare, or if the inflammation persists in spite of home care, or if the inflammation in the oral cavity is moderate to severe, then oral surgery to extract the premolars and molars and/or canines and incisors is recommended. The purpose of extraction is to lower the chronic antigenic stimulation from the plaque bacteria. Traditional medical therapy usually does not control the disease and resolve clinical signs. If there is no visible inflammation in the caudal buccal mucosal tissues or around the canine teeth and incisors then extraction of all of the premolars and molars is recommended. If there is periodontal disease or tooth resorption affecting the canine teeth and/or incisors they are extracted in addition to the premolars and molars. If there is inflammation involving the gingival tissue surrounding the canines and incisors or if there is inflammation in the caudal buccal mucosal tissues then initial oral surgery should be completed to extract *all* of the teeth.

With oral surgery it is essential to remove the entire tooth root. Full mouth radiographs *must* be obtained preoperatively. In each quadrant, a mucogingival flap is elevated and buccal bone is removed to expose the furcation of multi-rooted teeth. Each tooth is sectioned and the tooth roots are elevated and extracted. The alveolar bone should be smoothed with a diamond bur (alveoplasty). Each alveolus should be debrided and cleaned with either a diamond bur or hand curette to ensure removal of all tooth, root, and periodontal ligament and bone particles. Following extraction radiographs are obtained to confirm extraction of all tooth roots. NO tooth roots, root fragments or tooth remnants may remain. The periosteum of the flap is released and the alveolar gingival tissue is sutured to the lingual or palatal mucosal tissue utilizing absorbable sutures.

Pre-, intra- and postoperative analgesia is very important in these patients. Utilization of a multimodal preemptive pain management protocol is recommended.

If clinical symptoms persist after extraction of premolars and molars then the author recommends extraction of the remaining incisors and canine teeth to eliminate *all* plaque retentive surfaces. If inflammation still persists, then adjunctive medical treatment is recommended. Remember, most of these patients have had inflammation for a long time prior to presentation, so the inflammation within the oral cavity is not likely to resolve quickly after surgery. Medications may be necessary for an interim period while the patient's immune system responds. Frequent periodic monitoring of these patients is required to adjust medications and treatment based on each individual's response. There are no current studies to support the use of one particular medication over the others as the 'best' medical option.

Medical management of refractory cases

The primary goal of any treatment for a cat with gingivostomatitis is to decrease inflammation, pain, infection, and to modulate the host's immune response. Medical treatment is sometimes necessary *after* oral surgery to control disease in resistant cases.

Anti-inflammatory drugs

Use of these drugs as a sole treatment for cases with stomatitis is *not* recommended. Use of long term steroids can lead to diabetes mellitus and can decrease the body's ability to resist the inflammatory process. Often with long term use of steroids, cats seem to develop 'resistance' and their response to the drug decreases.

Prednisolone - 2 mg/kg daily for a week, then 1 mg/kg daily for a week then a maintenance dose of 0.5-1 mg/kg every other day (goal is to decrease to the lowest effective dose)

Oral triamcinolone - 1.5 mg per cat once daily for a week, then every other day for a week, then every 3 days. Then leave at twice a week for a few months and occasionally try weaning off medication. The pill can be crushed to a powder and suspended in water for administration.

Methylprednisolone acetate 15-20 mg/cat SQ every 3-6 weeks as needed

Antimicrobials

Use of antimicrobials will decrease the bacterial load in the oral cavity, but should *not* be utilized alone in cases of stomatitis. The most commonly used drugs include amoxicillin-clavulanic acid, clindamycin, doxycycline and metronidazole. Azithromycin has been suggested for use in Bartonella positive cats with gingivostomatitis. Studies by Dower and Quimby did not find any correlation between cats with gingivostomatitis and Bartonella and found treatment with azithromycin unrewarding. Chlorhexidine gluconate oral rinses have a bacteriostatic action, though most cats with a painful mouth resist oral rinses. Doxycycline has an inhibitory effect on the secretion of matrix metalloproteinases (which destroy collagen and other matrix components) by gingival PMNs. Use of a submicrobial dose may result in a decrease of gingival collagen destruction. This author has used a dose of 10 mg/cat twice daily for two weeks, then once daily for two weeks, then every other day if the patient shows clinical response. Some patients may require doxycycline at the lowest effective dose forever.

Immune modulating drugs

Cyclosporine is an immunosuppressant that focuses on cell mediated immune responses. While the exact mechanism of action is unknown, it is believed that it acts by a specific, reversible inhibition of immunocompetent lymphocytes in the G₀ or G₁ phase of the cell cycles. T-helper lymphocytes are the primary target, but T-suppressor cells are also affected. Lymphokine production and release (including interleukin-2, T-cell growth factor) are also inhibited by cyclosporine. Potential side effects include vomiting, diarrhea, hepatic dysfunction, impaired renal function, anemia, hypertrichosis, and gingival hyperplasia. Monitoring with complete blood counts and biochemistry profiles is recommended. Adjunct treatment with corticosteroids may be necessary.

Feline recombinant omega interferon (Virbagen Omega^R, Virbac) are immune modulating cytokines labeled for use in Europe to treat FeLV and/or FIV. It may also be of benefit in acute feline calicivirus infections and FIP. Its principle action is not as a direct anti-viral, but by acting on virus infected cells inhibiting mRNA and translation proteins, thereby inhibiting viral replication. Feline omega interferon has more antiviral effects against certain viruses than human alpha interferon. Virbagen Omega^R has been used in cats that are refractory to traditional treatments for gingivostomatitis. The therapeutic effect of interferon after oromucosal administration is due to the immunomodulatory activity through the oropharyngeal lymphoid tissues and via paracrine activity as this glycoprotein is destroyed during transit through the digestive tract. A randomized double blinded multicenter study was conducted studying calici positive cats presenting with persistent caudal stomatitis after dental extractions. The study showed that treatment with oral feline omega interferon resulted in significant clinical improvement and was found to be at least as good as short term prednisolone therapy in the treatment of calici virus positive cats presenting with caudal stomatitis after dental extractions. Virbagen Omega^R is not currently licensed for use in the US.

Other medical options

Lysine 250 - 500 mg/cat PO BID Lysine is an amino acid that is thought to compete with arginine for incorporation into many herpes viruses. As it is believed that arginine is required for producing infective virus particles, when lysine is incorporated the virus becomes less infective.

Niacinamide 500 mg ¼ tablet twice daily Used in canine medicine in combination with tetracycline to treat immune mediated skin conditions. It blocks IgE induced histamine release and degranulation of mast cells. When used with tetracycline it may suppress leukocyte chemotaxis secondary to complement activation by antibody antigen complexes. It also inhibits phosphodiesterases and decreases the release of proteases.

Esterified fatty acids

Esterified fatty acid complexes are administered orally and work transmucosally to modulate local inflammation.

Laser treatment

There is only one case study reporting the use of CO₂ laser treatment in a cat with gingivostomatitis. The study concluded that laser therapy is a viable adjunct, but should not be considered as a stand-alone modality or replacement for full mouth or nearly full mouth extractions. The goal of laser treatment is to remove the proliferative tissue to resolve the self-induced trauma and entrapment of food and debris in the tissue pockets; stimulate fibrosis to make the tissues less prone to continued inflammation and proliferation; and reduction of opportunistic bacteria. Laser treatment may also provide some pain relief as the surface nerve endings are cauterized.

Prognosis

Hennet studied the effectiveness of dental extractions: 60% of cats were clinically cured; 20% showed significant improvement with minor flare ups; 13% showed only little improvement and required continued medications; and 7% were refractory to treatment showing no improvement. A study of treatment outcome following full mouth extraction published by Girard in 2005 showed 50% resolved without further treatment, 37% improved but required continuing medical treatment and 13% did not improve. There is

continuing discussion regarding which teeth should be extracted - all premolars and molars only or extraction of all teeth (including canine teeth and incisors). There is currently no published data to support either treatment modality.

Owners of cats with stomatitis should understand that not all cats respond to treatment and this disease is often frustrating to treat. It requires consistent treatment and frequent monitoring of the cat's response to treatment.