Masticatory Muscle Myositis in a Golden Retriever

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Summary

Sunny, a 1 ½ year-old female spayed Golden Retriever, presented to her referring veterinarian in January 2009 for pain and swelling around the right eye. The veterinarian prescribed an antibiotic and a glucocorticoid which resolved the dog's pain and swelling. In March, she presented for difficulty with prehending food. On sedated oral exam, it was found that she had drastically reduced range of motion of her jaw. Upon recovery from sedation, her tongue became entrapped between her carnassial teeth on the right side.

Sunny presented to the CUHA Emergency and Critical Care Service on March 12, 2009 for evaluation of her reduced mandibular jaw range of motion and therapy for the entrapped tongue. On presentation, Sunny was bright and alert. She was panting, but otherwise, her vital parameters were within normal limits. Her temporal and masseter muscles were atrophied and her saggital crest prominent. Her mandibular jaw range of motion was 3 cm from measured from the maxillary central incisor tip to mandibular central incisor tip. Her tongue was protruding from the left side of her mouth to the level of the frenulum. It was significantly swollen with a soft fluctuant area around the frenulum. The tip of the tongue was dry but not discolored. Other physical exam findings included a cranial drawer sign in the left stifle and a BCS of 7/9.

Sunny was admitted to the hospital that evening and a tracheostomy was performed due to airway restriction caused by the lingual swelling. Feline Finochietto rib spreaders were placed between her incisors and slowly opened over the night to free the tongue and increase mandibular jaw movement. Steroid therapy was initiated. The following morning, Sunny's tongue was placed back in her mouth. A CT-scan of her head was performed, and muscle biopsies were taken from her temporal and masseter muscles on the left side. The CT-scan showed atrophy of the temporal and masseter muscles on the right side and swelling of those muscles on the left. Blood was also submitted for a Type 2M autoantibody test. Her 2M antibody test was positive (1:400) and her muscle biopsies were also positive for masticatory muscle myositis.

Sunny was started on immunosuppressive doses of prednisone (50mg BID). She regained the ability to prehend food within a few days. She was discharged to the care of her owners with instructions to feed soft food, and a diet was initiated to decrease the strain on her injured stifle. Sunny's masticatory muscles responded well to the prednisone and she slowly regained acceptable range of motion of her jaw. She is now able to eat normal food and play with her toys. She currently has both cranial cruciate ligaments ruptured. Her steroid dose has been tapered down to 5mg BID and she has been lost to follow-up.

Masticatory muscle myositis is an autoimmune disorder that affects dogs. Autoantibodies are formed that are specific to type 2M myofibers. These myofibers are found only within the dorsal group of muscles innervated by the mandibular nerve. These muscles include the temporalis, masseter, pterygoideus, tensor veli palatini and tensor tympani muscles. Clinically, the disease manifests as an inflammatory stage where there is an active immune reaction to the 2M myofibers, followed by fibrosing of the myofibers where the necrotic muscle is replaced by collagen.

Signalment

Sunny is a 1 1/2 year old female spayed Golden Retriever.

Chief Complaint

Sunny was presented to the CUHA Emergency and Critical Care service on March 12, 2009 for evaluation of trismus, protrusion of her tongue and lingual entrapment. The base of her tongue had become entrapped between the mandibular and maxillary molars on the left side of her mouth.

Case History

Sunny was originally presented to referring veterinarian on January 20, 2009 with a history of swelling around the eye and in the area of the forehead on the right side, and pain. At that time, it was assumed that Sunny had some sort of infection and it was treated and resolved with prednisone and Clavamox administration. The swelling reappeared once the medications were discontinued. At the time of the recheck exam, Sunny's medical record shows that her face appeared normal and was non-painful on examination. Her family elected to continue to monitor her at home.

On March 9, 2009, Sunny was taken back to her referring veterinarian with a 2 week history of drooling, difficulty eating, left-sided facial swelling, and decreased activity. On examination it was found that she was febrile and unable to open her mouth. She was administered Meloxicam subcutaneously, and discharged with prescriptions for oral Meloxicam and Clavamox, but the owner reports she never administered the Clavamox to Sunny. Two days later, on re-check examination March 11th, Sunny was reported to have improved, but was still having difficulty eating. The owners reported that she was taking excessive time to finish a meal (she was normally a very fast eater) with food frequently observed to fall out of her mouth.

The next day, March 12, Sunny was placed under general anesthesia for an oral examination and radiographs of the head and left stifle were also obtained. It was noted while under anesthesia that Sunny's jaw was "locked," and a complete rupture of the left cranial cruciate

ligament was diagnosed based on a positive cranial drawer and tibial thrust tests. While under anesthesia, Sunny's tongue had slipped out of her mouth on the left side, and upon awakening from anesthesia, the tongue became entrapped between her carnassial teeth and was unable to be replaced in her mouth. She was brought to the CUHA Emergency and Critical Care Service approximately 12 hours later when her tongue was still entrapped and had become swollen and dry.

Clinical Findings

On presentation, Sunny was bright and alert. Her tongue was protruding from the left side of her mouth. It was entrapped between her carnassial teeth and the frenulum was visible external to the mouth. There was a large, fluid-filled swelling on the underside of the tongue in the area of the frenulum. Sunny was also mildly lame in the left hind limb. Her body condition score was estimated at 7/9. Her temporal muscles were atrophied bilaterally, with the saggital crest appearing prominent.

On physical examination, Sunny was observed to have a good haircoat with no signs of ectoparasites. No skin lesions or masses were seen. Her ears were pink and free of debris. She had no nasal or ocular discharge and no abnormalities on fundic exam. No cough was elicited on tracheal palpation. Her mandibular, superficial cervical and popliteal lymph nodes were not palpably enlarged or painful. Her mucous membranes were pink and slightly tacky and her capillary refill time was less than two seconds. She had strong femoral pulses and no cardiac murmurs or arrhythmias were noted on auscultation. Sunny was panting heavily, but normal lung sounds were ausculted over all fields with no crackles or wheezes evident. On abdominal palpation, Sunny's abdomen was soft and nonpainful and no abnormalities were noted. She had a cranial drawer sign in her left stifle, with no other joint pain or effusion noted. Sunny's tongue

appeared pink and was slightly dry. There was an erythematous and fluctuant swelling on the underside of the tongue, but no black discoloration or areas of necrosis were observed.

Sunny was placed under general anesthesia and a tracheostomy was performed. The fluctuant swelling beneath her tongue was drained using a needle and syringe. A moderate volume of serosanguinous fluid was removed. Finochietto rib spreaders were placed between Sunny's incisors and opened to try to increase her range of motion. Sunny remained under anesthesia throughout the night. She was started on IV Dexamethasone and Unasyn. Her tongue was alternately soaked in a 50% Dextrose solution and iced overnight to reduce the swelling. The next day, her tongue was replaced into her mouth. Her interincisor distance was measured at 2cm. A 2M autoantibody titer test was submitted, a CT scan was taken of her head, and muscle biopsies of her temporal muscles were performed.

Problem List

Trismus

Bilateral Temporal Muscle Atrophy

Entrapped, Protruding Tongue

Left Stifle Cranial Drawer Sign

Differential Diagnosis

Trismus:

- Degenerative
  - Temporomandibular Joint Osteoarthritis
- Anomalous
  - Craniomandibular Osteopathy, Muscular Dystrophy, Myotonia Congenita, "Scotty Cramps"
- Metabolic
  - None
- Neoplasia/Nutrition
  - Osteosarcoma, Chondrosarcoma, Squamous Cell Carcinoma, Melanoma, Adenocarcinoma, etc. associated with bone near TMJ or the TMJ itself
- Infectious/Inflammatory/Immune-Mediated

        - Masticatory Muscle Myositis, TMJ Synovitis, Neosporosis, Dermatomyositis, Polymyositis, Tetanus, Buccal/Retrobulbar Abscess, Otitis Externa/Media, Sialadenitis
- Toxin/Trauma
    - Fracture of Maxilla/Mandible, TMJ Ankylosis/Pseudoankylosis

Temporal Muscle Atrophy:
- Degenerative
    - Neurogenic Atrophy, Disuse Atrophy, Cardiac Cachexia
- Anomalous
    - Muscular Dystrophy, Exocrine Pancreatic Insufficiency
- Metabolic
    - Addison's Disease
- Neoplasia/Nutrition
    - Any Neoplasia, Malnutrition
- Inflammatory/Infectious/Immune-Mediated
    - Masticatory Muscle Myositis, Polymyositis, Dermatomyositis, Inflammatory Bowel Disease
- Toxin/Trauma
    - None

Combined:
TMJ Disorder, Muscular Dystrophy, Neoplasia, Masticatory Muscle Myositis, Polymyositis, Dermatomyositis

Due to Sunny's signalment and the fact that her muscle atrophy appeared to be confined to the masticatory muscles, and the lack of other clinical signs, the most likely diagnosis was Masticatory Muscle Myositis.

Diagnosis

Imaging:

Sunny's referring veterinarian took oblique skull radiographs to view the temporomandibular joint, as well as the dental arcades and associated structures. A CT scan was performed at the CUHA to evaluate the bony structures of the head in more detail and also to evaluate the soft tissue structures pre- and post-contrast. The skull radiographs from the referring veterinarian showed no abnormalities. The CT scan showed no bony abnormalities. The right

temporal and masseter muscles were mildly atrophied, while those on the left appeared swollen and had heterogeneous contrast uptake indicating active inflammation. Her mandibular, medial retropharyngeal and parotid lymph nodes were bilaterally enlarged with mild contrast enhancement.

Radiography is a useful tool for evaluation of trismus. It can be used to rule down or rule out many bony causes for trismus in a dog. Mandibular and maxillary fractures are readily seen on radiographs. Likewise, a bony neoplasia and craniomandibular osteopathy would be apparent. Disorders that directly affect the TMJ are more difficult to view on plain radiographs, but some abnormalities associated with the joint may be seen in disorders such as TMJ osteoarthritis, synovitis, and ankylosis/pseudoankylosis. Disorders that affect the soft tissues such as myosidities, infectious diseases, abscesses, muscular dystrophy and myotonia congenital may not be readily apparent on radiographs.

In order for radiographs of the skull to be the most effective, several views should be taken. The skull is difficult to radiograph due to the summation of the bony calvarium with the surrounding structures. Also, there are many different skull conformations among the different dog breeds. Different views help to view the surrounding structures individually without the calvarium interfering with the views. A dorsoventral view of the skull is useful to evaluate the symmetry between the two temporomandibular joints and to see the joint space. Lateral views are generally not useful due to superimposition of the two TMJs upon each other. Oblique views can be useful to individually evaluate the TMJs, and also to remove the summation due to the skull. An Lt45°V-RtDO or Rt45°V-LtDO view allows an unimpeded view of the down TMJ, and a view of the up TMJ that is superimposed with the skull. This view is accomplished by placing the animal in lateral recumbency and rotating the patient's skull 45° about its long axis. A Rt20°Ro-LtCdO or Lt20°Ro-RtCdO ("nose-up" view) can also be used to image the TMJs. This view is

accomplished by laying the patient in lateral recumbency and raising the nose approximately 20° off the table using a foam pad. The lower TMJ may be superimposed over the base of the skull in this view.[8] These 5 views allow for evaluation of the TMJs from different angle to best observe any pathology associated with the joints and their surrounding structures.[8]

MRI and CT are advanced imaging modalities that can provide more information than plain radiographs in the diagnosis of TMJ disorders, as well as soft tissue disorders causing trismus. MRI is a better modality for the assessment of soft tissue pathology but has not been well characterized in the use of diseases causing trismus in dogs and cats.[8] Computed tomography is a modality has been studied in cases of masticatory muscle myositis, and the CT changes associated with the disease have been characterized. The changes most often associated with the inflammation, necrosis and fibrosis of the masticatory muscles include change in size (swelling or atrophy), heterogeneous pattern of contrast enhancement, precontrast hypoattenuation in some cases, and enlarged head and neck lymph nodes.[7] CT is not useful as a diagnostic test, as any process resulting in inflammation and fibrosis can cause this pattern of changes. However, it is a useful tool in helping to rule out other causes of trismus, as well as selecting a site for muscle biopsy.[7]

2M Autoantibody Test:

Masticatory muscle myositis is an autoimmune disease where the animal's immune system produces antibodies to the myosin specific to the masticatory muscles. The masticatory muscle group contains a unique 2M fiber type that is not found in the limb muscles,[2] where type 2C muscle fibers predominate. The type 2M fibers have a myosin isoform with unique heavy and light chains.[17] This myosin isoform is the target of autoantibodies in the disease. The etiology of the disease process is unknown, but has been speculated to be a result of an infectious agent

whose antigens closely resemble the 2M fibers, or secondary to trauma of the masticatory muscles, or to be genetically determined in certain breeds.[7, 8] Most recently, it has been found that the myosin fiber that is targeted by the autoantibodies colocalizes with dystrophin close to the cell surface which may make it accessible as an immunogen.[4] The 2M autoantibody test is run on serum from an affected dog. It tests for the presence of circulating antibodies to the unique myofibers. The test is an ELISA using the masticatory muscle myosin as the antigen.[17] The test is 85-90% sensitive and 100% specific.[10] False negative results are possible if the dog has been administered corticosteroids prior to testing, or if the dog is in the chronic phase of the disease where the immune-mediated destruction has decreased and fibrosis predominates.[1]

Muscle Biopsy:

The definitive test for masticatory muscle myositis is a biopsy of the affected muscle and histopathology. As previously stated, CT can be used to choose an ideal location for sampling. A sample from a muscle that appears to be actively inflamed is preferred. On histopathology, affected masticatory muscles have infiltration by predominantly B cells, dendritic cells and macrophages. There are also more $CD4^+$ T cells than $CD8^+$ T cells and MHC class I and II are expressed on the surface of the muscle fibers.[3, 6, 17] The infiltration of immune cells is most commonly perivascular. Also seen on histopathology is atrophy of the muscle fibers and fibrosis. The fibrosis in masticatory muscle myositis is both endomysial and perimysial. End-stage fibrosis is characterized by complete loss of muscle fibers with replacement by connective tissue.[18]

Prognosis

Masticatory muscle myositis is not a fatal disease. Trismus is a potentially life-threatening complication of the disease that can lead to the inability to eat. The prognosis for return to function in a dog that is diagnosed in the acute phase and treatment is initiated promptly is good.

The damage to the muscle tissue is reversible and the function of the TMJ will not be impaired. In a dog that is diagnosed in the end stage and already has severe fibrosis, the prognosis for return to function is not good. The fibrosis is generally not reversible. A feeding tube can be placed in these dogs to maintain quality of life and they can do well long term. Dogs in between these two stages that are treated generally have some improvement in function but remain affected to some degree for life.

Treatment

The treatment of masticatory muscle myositis is aimed at dampening the immune response to self-antigens. Glucocorticoid therapy is the mainstay of treatment against the disease. 1-2mg/kg of prednisone is the starting dose for treatment. The prednisone should be slowly tapered over 8-12 months to the lowest dosage without return of clinical signs.[1] Affected dogs generally improve rapidly once glucocorticoid therapy is initiated.

Other immunomodulatory drugs such as Mycophenolate and Azathioprine could potentially be used to manage the disease. These drugs have not been well studied in masticatory muscle myositis, and any statements of efficacy that exist are purely anecdotal. However, their successful use in other autoimmune diseases would indicate that they may be useful in conjunction with glucocorticoids to manage the disease and decrease the side effects seen at high doses of glucocorticoids.

As stated before, B cells are the predominant cell type infiltrating the muscle fibers in masticatory muscle myositis. B cells are responsible for producing the antibodies that bind the autoantigens and initiate the immune response. Therefore, it has been suggested that anti-B cell therapy may be efficacious in managing the disease.[11]

The fibrosis of the masticatory muscles generally does not reverse with initiation of glucocorticoid therapy. Antifibrotic agents such as colchicine have been used in the management of the disease. There are no scientific studies that investigate the efficacy of this therapy. It may be more useful to prevent new production of connective tissue rather than destroying connective tissue that has already been formed.

Mechanical breakdown of the fibrotic tissue is another method of treatment that has been used. There is anecdotal evidence that this is an effective treatment, but no published data. The breakdown is accomplished by inserting increasing numbers of tongue depressors between the teeth to slowly wedge the jaw open. It is best to place the tongue depressors behind the carnassial teeth to prevent fracture of the more delicate premolars and incisors.

Outcome

At the time of her discharge from the hospital, Sunny's interincisor distance was measured at 3cm. Sunny was started on a 2mg/kg dose of prednisone twice a day. At her two week recheck appointment, her interincisor distance had increased to 4cm and her tongue appeared normal. Physical therapy with chewy toys was initiated to help rebuild her atrophied masticatory muscles. A soaked kibble diet was initiated following this visit.

Her interincisor distance remained 4cm at her one month recheck. Her prednisone dose was decreased to 1mg/kg twice a day. After two months, her interincisor distance was 4.5cm and her prednisone dose was further decreased to 0.5mg/kg. Finally, at her three month recheck it was decreased to 0.25mg/kg twice a day. At that time, Sunny was experiencing lameness due to bilateral cruciate ligament rupture and hip dysplasia. She was also experiencing GI upset. After her three month recheck, Sunny continued to do well and was lost to follow-up.

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