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MEGAESOPHAGUS AND OTHER CAUSES OF ESOPHAGEAL DILATION

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ANATOMY AND PHYSIOLOGY

The esophagus is a hollow muscular tube transporting liquid and ingesta to the stomach. It consists of the upper esophageal sphincter (UES), the tubular esophagus, and the lower esophageal sphincter (LES). The entire length of the canine esophagus is composed of striated muscle (the smooth lamina muscularis mucosae does not contribute to peristalsis), whereas the distal one third of the feline esophagus is composed of smooth muscle. The lining of the esophagus is a robust stratified squamous epithelium which terminates abruptly at the point of entry into the stomach into a simple columnar lining. Unlike most other parts of the GI tract, coordinated motor function depends on an extrinsic nervous system; the vagus nerve and associated branches innervate the esophagus. The neural coordination contains somatic motor nerves from the brain stem nucleus ambiguus to the esophageal striated muscle, autonomic nerves to the esophageal smooth muscle, and general visceral afferent nerves from the esophageal sensory receptors. The esophageal phase of swallowing begins with relaxation of the UES, thus moving the food bolus into the proximal esophagus. The first peristaltic wave generated in the pharynx carries the bolus further aborally (primary peristalsis). If the primary peristalsis is insufficient to propel the bolus into the stomach, a second peristaltic wave is generated by esophageal distension-sensitive receptors that complete bolus transport. The LES relaxes in advance of these pressures and contracts again after the bolus has passed, thereby preventing reflux of gastric contents.

MEGAESOPHAGUS

The term megaesophagus (ME) describes a syndrome of segmental or diffuse dilatation of the esophagus due to several causes including hypomotility and loss of normal peristaltic activity or obstruction. It is a consequence of esophageal disease and not a disorder in itself (a better term would be *esophageal hypomotility*). ME may be congenital or acquired, and it may be primary/idiopathic or occur secondarily to a number of causes. The underlying pathomechanism is unclear, but a dysfunction within the afferent vagal arm of the swallowing reflex is suspected.

CLINICAL SIGNS

Regurgitation is the hallmark clinical sign noted with ME. Frequency and timing of regurgitation after feeding can vary considerably. Some owners also report vomiting. Weight loss and poor body condition is seen with chronic disease. Respiratory problems (cough, dyspnea) occur secondary to aspiration pneumonia, which is a common complication. Additional clinical signs detected in dogs with acquired secondary ME might be weakness and gait abnormalities with polymyopathies, exercise intolerance with neuromuscular disease, or GI signs with Addison's disease.

DIAGNOSIS

Diagnosis of ME/esophageal dilation is based on a history of regurgitation and radiographic demonstration of esophageal dilatation followed by diagnostic evaluation to rule out secondary causes. Esophageal dilatation can be caused by excitement, aerophagia, sedation / general anaesthesia, cough or persistent vomiting. Although in these situations dilatation is normally mild. The finding of persistent esophageal dilatation visualized on serial radiographs is more reliable. Dogs with idiopathic ME tend to have more marked radiographic esophageal dilatation, than do dogs with other causes of ME. The presence of pulmonary alveolar opacities indicates aspiration pneumonia. The relative prevalence of different causes of ME is unknown, but there is general agreement that the idiopathic form is most common. Breeds commonly diagnosed with idiopathic ME are Golden Retrievers, Labrador Retrievers, and German Shepherds, but any breed may be affected.

CONGENITAL MEGAESOPHAGUS / REGURGITATION AT A YOUNG AGE

Congenital idiopathic ME is known to be inherited in the wire-haired Fox Terrier and Miniature Schnauzer. It has also been documented in Parson Russell Terriers, Springer Spaniels and Samoyeds. Predisposed breeds in the author's institution are Irish Setters, Labrador Retrievers, the Berger Blanc Suisse (White German Shepherd), Groenendaels, and German Shepherds. With congenital disease, puppies are usually presented around 5-6 weeks of age. Physical examination is usually unremarkable with the exception of a decrease in average daily weight compared to littermates. Radiographically the esophagus can be mildly to markedly dilated. Treatment usually consists of small frequent meals from an upright position to assist passage of ingesta into the stomach. It is the author's firm belief, that the upright position is superior to feeding from an elevated position. Ideally these dogs are held like this for another 20-30 minutes. The more these young patients are malnourished, the less they are likely to improve clinically. A treatable differential at a young age is a vascular ring anomaly (persistent right aortic arch, PRAA), as it will cause esophageal dilation in puppies. It should be considered when regurgitation starts at the time of weaning off the mother's milk. Breeds more commonly affected include the Great Dane, German Shepherd, and Irish Setter. The diagnosis is usually straightforward using plain chest radiographs and contrast esophagrams are not necessary to confirm the diagnosis of vascular ring compression. Focal leftward deviation of the trachea near the cranial border of the heart in DV or VD radiographs is a reliable sign of PRAA in young dogs that regurgitate after eating solid food.² Most dogs undergoing surgery to correct this condition will have resolution of the regurgitation and thrive well.

Rarely, ME occurs in conjunction with congenital myasthenia gravis (MG), usually with concurrent generalised muscle weakness. This has been reported in Jack Russell Terriers, Springer Spaniels, Smooth Fox Terriers, and smooth-haired Miniature Dachshunds. Congenital MG results from a congenital deficiency of acetylcholine receptors (AChRs) and thus affected dogs do not have measurable circulating anti-AChR antibodies. A diagnosis of congenital MG is based on clinical signs, results of

electrophysiological testing, and response to the short-acting anticholinesterase drug, edrophonium chloride. Demonstration of decreased AChR density in muscle biopsies can help to confirm the suspicion. Symptomatic treatment should be tried, as affected dogs can have spontaneous remission and complete recovery.³ Finally some puppies and young dogs present with regurgitation, but lacking radiographic evidence of ME. Esophageal dysmotility (general or segmental) without overt ME occurs in young Terrier breeds, but can also be seen in other breeds.⁴ Improvement in esophageal motility occurs with time in some dogs, and might represent a syndrome of delayed esophageal maturation. Similar results of fluoroscopic esophageal motility improvement have been reported in Chinese Shar Pei pups.⁵ Indeed, the canine esophagus can demonstrate postnatal maturation up to 1 year of age. Improvement of esophageal function with age is thought to be attributed to maturation of the neuromuscular system of the esophagus. The author strongly believes that it is reasonable to offer symptomatic treatment for puppies with esophageal disease, as the prognosis for improvement may be favorable in some cases.

ACQUIRED SECONDARY MEGAESOPHAGUS

Acquired secondary ME/ esophageal dilation may result from many disorders, especially diseases causing diffuse neuromuscular dysfunction. The so-called idiopathic ME also falls in the category of neuromuscular disease, but remains a diagnosis of exclusion, as the underlying defects are yet unknown.

Dogs with **Myasthenia gravis (MG)** usually account for the biggest proportion (~ 25-30%) of patients with acquired ME.⁶⁻⁸ Acquired MG is mostly seen in dogs between 2-4 years of age or older than 9 years. German Shepherds and Golden Retrievers are most commonly affected, but Akitas and Scottish terriers also have an increased risk for MG. Affected cat breeds include the Abyssinian, Somali, and Siamese. Many dogs diagnosed as idiopathic ME, may actually have focal MG. One third of 152 dogs originally diagnosed with idiopathic ME that were retested either had a positive AChR antibody titer or a positive immunocytochemical staining, and 48% improved clinically with cholinergic therapy.⁸ Because MG may mimic idiopathic ME, testing should be performed in all dogs with esophageal hypomotility, even in the absence of generalized muscle weakness.

Interestingly, less of an esophageal dilatation is seen radiographically in myasthenic dogs with ME than in dogs with other causes of ME. Even though the *relative esophageal diameter* (defined as the ratio of the maximum esophageal diameter measured divided by the diameter of the thoracic inlet) was significantly smaller in myasthenic dogs in one study, it cannot be used as a screening test for ME due to acquired MG, as there was a large overlap between groups.⁶

Polymyositis/polymyopathy is another neuromuscular differential diagnosis for esophageal hypomotility. This is why a serum CK measurement should always be part of the minimal data base in these patients.

Myalgia is rarely described in polymyositic dogs, predominant clinical signs are generalized weakness, stilted gait, dysphagia, muscle atrophy, and dysphonia. Boxers and Newfoundlands were overrepresented in a large study on inflammatory myopathies and ME was more commonly seen in Newfoundlands.⁹ Interestingly the Newfoundland breed also has a genetic predisposition for MG.¹⁰ It is also the author's experience in Switzerland, that boxers seem predisposed for inflammatory myopathies associated with esophageal hypomotility. A properly performed muscle biopsy (and in some cases peripheral nerve biopsy) is essential to the diagnosis.

Dysautonomia refers to a generalized degenerative dysfunction of the autonomic nervous system of dogs and cats and is primarily seen in the mid-western United States (Missouri, Kansas). It is pathologically characterized by chromatolytic degeneration of the neurons in the autonomic nervous ganglia that results in clinical signs related to dysfunction or failure of the vegetative autonomic nervous system (parasympathetic > sympathetic nervous systems). Clinical signs include gastrointestinal and urinary bladder dysfunction, as well as ocular signs (mydriasis, decreased tear production, dry mucous membranes and decreased or absent anal tone). Common radiographic findings of dysautonomia include ME, aspiration pneumonia, gas or fluid distension of the stomach (gastric motility should not be impaired with myasthenia gravis) or small bowel, and a severely distended urinary bladder. When taken in context with the clinical signs of the patient, any combination of these findings should result in dysautonomia being added to the list of differential diagnoses, and patients should undergo pharmacologic testing (pilocarpin test, bethanechol test) to help confirm a diagnosis.

ME associated with **distemper** is due to demyelination. Clinically important is that neurologic signs can still develop weeks or months after initial recovery.¹¹ Nerve damage is due to an inflammatory response to the viral antigens in neurons and glial cells. Generalized **tetanus** can also cause ME and esophageal dysfunction. These patients most often have a stiff gait and a joker's smile/risus sardonicus (erect ears, drawn-back lips, and wrinkled forehead).

Endocrine causes – Although a rare finding, **Addison's disease** may cause ME in dogs. Electrolyte imbalance may result in decreased neuromuscular function, but mild esophageal dilations are also seen in Addisonians with normal electrolytes. Sole cortisol deficiency may lead to an impaired carbohydrate metabolism of myocytes and depletion of muscular glycogen. It is most likely the same reason that some owners are concerned about perceived musculoskeletal pain in their dogs. Because normal electrolytes do not rule out hypoadrenocorticism, a baseline serum cortisol should be included in the work-up of dogs with ME. Baseline cortisol values above 2 mcg/dl are sufficient to rule out an underlying hypoadrenocorticism. The association between **hypothyroidism** and ME is more controversial, as results of a larger case-controlled study did not show associations between both entities.⁷ However, reversible ME in hypothyroid dogs with complete clinical and radiographic recovery once the thyroid is regulated have been reported.^{12,13}

Gastrointestinal causes associated with acquired ME include esophagitis, esophageal obstruction, and hiatal hernias. **Esophagitis** may lead to mild esophageal dilations on radiographs. Often gastroesophageal acid reflux due to an incompetent LES is suspected to cause esophagitis in pets. However more common scenarios for increased esophageal acid exposure in small animals are lodged foreign bodies, frequent vomiting, malpositioned

esophageal feeding tubes and aggressive gastric factors (gastric acidity, volume, and duodenal contents) associated with delayed gastric emptying. It is important to note that independent of the cause of the esophagitis, esophageal inflammation in itself may cause esophageal hypomotility and LES weakness by impairing the excitatory cholinergic pathways to the LES. In cats, induction of experimental esophagitis attenuated the release of acetylcholine and lowered LES pressures. These changes were reversible on healing of the esophagus.¹⁴

Esophageal obstruction with secondary esophageal dilation can be caused by foreign bodies, neoplasia, and strictures (post pill esophagitis). Although certainly possible in any dog, the author sees esophageal foreign bodies often in West Highland White Terriers (WHWT) and Cairn Terriers of any age. In Zurich, chest radiographs are taken in any WHWT that is presented with signs like a sudden onset of vomiting, drooling, suspicion of pain, or panting in order to assess the esophagus. As pointed out above, these dogs may have an underlying tubular esophageal motility disorder. It is also important to note that a foreign body should never be ruled out based on the observation that the patient is still seen eating, as some foreign bodies may only cause partial obstruction. Esophageal foreign bodies must be removed ASAP, because ulcerative damage that penetrates into the lamina muscularis causes inflammation likely resulting in fibrous connective tissue strictures.

Hiatal hernias cause a radiographically dilated esophagus because they diminish the pressure topography of the gastro-esophageal junction by reducing its maximal pressure. This in turn facilitates an increase in gastroesophageal reflux and can cause reflux-esophagitis; the esophageal inflammation augments in return hypomotility. This is why medical therapy with proton pump inhibitors is suggested prior to phrenoplasty and esophagopexy. Hiatal hernias are more often seen in Chinese Shar Peis and French Bulldogs.

ME as a paraneoplastic syndrome is seen in canine and less common in feline **thymomas**. The thymic masses appear radiographically as large soft tissue masses in the cranial mediastinum. Surgical resection of neoplastic tissue can lead to resolution of myasthenic signs (including ME). **Toxins that can cause ME include lead, organophosphates, and thallium.** Lead ingestion causes gastrointestinal signs and ME results from a vagal polyneuropathy. Lead toxicity can occur from ingestion of linoleum, fishing line weights or batteries. Increased amounts of nucleated erythrocytes without anemia and basophilic stippling may be seen on blood smear evaluation. Organophosphates exist in flea collars and pesticides and they bind to acetylcholinesterase, causing cholinergic overstimulation (lacrimation, salivation, urination, defecation). Thallium is used in semiconductors and optical lenses and thallium toxicity in dogs causes gastrointestinal signs initially, followed by alopecia, peripheral neuropathies and gradual onset of ME.¹⁵

ESOPHAGEAL NEOPLASIA

Although esophageal tumors are very rare in cats and dogs, esophageal leiomyoma can radiographically and clinically mimic ME.^{16,17} Diagnosis is based on esophagoscopy or contrast esophagram. Cases of complete recovery after surgical resection have been described.

IDIOPATHIC MEGAESOPHAGUS

It has been suggested that the responsible lesion is located in the vagal afferent innervation to the esophagus in the majority of dogs with idiopathic megaesophagus¹, however esophageal achalasia has also been reported.¹⁸ Esophageal achalasia is characterized by failure of the LES to relax adequately, increased LES tone, and later in the course of the disease lack of esophageal peristalsis. Diagnosis is based on barium esophagram showing esophageal contraction against a LES, that fails to relax and open, or esophageal manometry. Resolution of clinical signs and radiographic abnormalities after esophagomyotomy have been described in single cases.^{18,19}

TREATMENT

Patients with acquired ME require treatment of the underlying specific disease next to supportive care. The primary goal is to meet the nutritional needs and minimize regurgitation. Feeding frequent high-caloric meals from an upright position helps move the ingesta into the stomach. Because it is very difficult for owners to keep their medium to large-sized dogs in a vertical position for at least 20-30 minutes after feeding, a special chair (i.e. *Bailey chair*) in which the dog can virtually sit upright on his hindlegs during the postprandial phase should be recommended. It is the author's experience that only those dogs fed in an upright position survive longterm. Food consistency should be varied, to determine individually what works best. Severely malnourished dogs benefit from a gastrostomy tube (PEG followed by low profile tube) and some dogs go on living with a permanent gastrostomy tube. Aspiration pneumonia is treated with broad (or 4-quadrant) spectrum antibiotics and need to be given IV in severely debilitated patients. It has been suggested that esophagitis is a common complication of ME. This may hold true for ME secondary to MG, polymyopathies, or hypoadrenocorticism. However this may not be the case in the idiopathic form, where LES tone seems rather tense. If esophagitis is still suspected, treatment consists of sucralfate and proton pump inhibitors (H₂-blockers such as ranitidine and famotidine are less effective). Prokinetic drugs (cisapride, metoclopramide) have no effect on striated muscle and therefore no benefit in managing canine ME. In contrast they increase LES pressure and may hinder esophageal emptying and worsen regurgitation. Cats with ME may benefit from cisapride, as their distal esophagus is composed of smooth muscle.

PROGNOSIS

Of course the prognosis varies with the underlying disease and especially the presence of complications such as aspiration pneumonia or malnutrition. An important factor that has never been critically evaluated in the literature is owner dedication and commitment. Generally congenital ME has a guarded prognosis, but it is impossible to predict future improvements of esophageal motility at the time of diagnosis. Spontaneous remission of acquired MG with resolution of ME can occur within 6 months.²⁰ Acquired idiopathic ME also has a guarded to poor prognosis, usually because of the combination of aspiration pneumonia and malnutrition. Nevertheless, it is surprising how variable the course of disease is in dogs that survive the critical phase and again this is closely related to owner commitment. In a recent study analyzing clinical factors associated with death before discharge and overall survival time in dogs with ME only radiographic evidence of aspiration pneumonia and the age at

onset of clinical signs were significantly associated with survival.²¹ Dogs > 13 months old at the time of onset of clinical signs were 6.4 times as likely to die at a given time point as were dogs ≤ 13 months old. Also more marked esophageal dilation was not associated with a poorer prognosis in that study.

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