Update on Feline Asthma

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KEYWORDS

• Feline asthma • Feline lower airway disease • Airway eosinophilia
• Airway hyperresponsiveness

KEY POINTS

- Feline asthma is an important chronic lower airway disease of cats; however, definitive diagnosis is challenging because of overlapping clinicopathologic features with other lower airway disorders.
- Discriminating asthma from other chronic lower airway diseases (eg, infectious or chronic bronchitis or a variety of parasitic infections) is necessary because of differences in pathogenesis, novel treatments, and prognosis.
- Emerging diagnostics including thoracic CT scans and pulmonary function testing may help differentiate feline asthma from other chronic lower airway diseases.
- Therapy for feline asthma using glucocorticoids and bronchodilators might be inadequate or contraindicated in some cats; novel treatments investigated in experimental models of feline asthma could be beneficial in refractory cases or as adjuncts for glucocorticoid-sparing effects.

INTRODUCTION

Asthma is a common lower airway inflammatory disease in cats thought to be allergic in cause.[1] It is most commonly treated with glucocorticoids and bronchodilators. Although these are effective treatments in many cats, some cats are unresponsive or minimally responsive. In addition, chronic glucocorticoid therapy might not be well tolerated or could be contraindicated with certain diseases, such as diabetes mellitus or congestive heart failure. Finally, these therapies fail to reverse the abnormal immune response and ultimately do not ameliorate chronic airway remodeling that results in declining lung function. New therapies capable of restoring immune tolerance, acting more selectively to diminish allergic immune dysfunction with minimal systemic effects, or blunting airway remodeling would be desirable. Evaluation of novel

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therapeutics in clinical trials of pet cats with asthma is hindered by a lack of consensus on what defines asthma and how it can be discriminated from other lower airway disorders. Thus, development of additional diagnostic tests in this arena is sorely needed. This article reviews what is currently known regarding the diagnosis and treatment of feline asthma as well as several new diagnostics and treatments that are on the horizon.

EPIDEMIOLOGY

Defining epidemiologic factors in feline asthma is complicated by a lack of consensus regarding what defines asthma in cats and how in practice it is best discriminated from other disorders. Most published studies fail to discriminate spontaneous feline asthma from chronic bronchitis, combining information from both disorders. Feline asthma is estimated to affect approximately 1% to 5% of the feline population.[2] Although the median age at presentation is 4 to 5 years, many cats have a history of chronic signs, suggesting that disease onset occurs much earlier in life.[3–5] There is no clear gender predilection.[3–7] The Siamese breed is overrepresented in some studies,[3,7] but not others.[4,6]

PATHOGENESIS

Evidence that asthma is mediated by an allergic response after exposure to inhaled aeroallergens is reviewed in detail elsewhere.[1] Aeroallergen-induced stimulation of a T helper 2 response leads to elaboration of a variety of cytokines. These cytokines drive the molecular switches that lead to pathologic changes in the airways. The 3 major hallmark features of asthma extrapolated from the disease in humans include airway inflammation, airway hyperresponsiveness and airflow limitation (the latter being at least in part reversible), and airway remodeling.[8]

PATIENT HISTORY AND PHYSICAL EXAMINATION

Clinical signs of feline asthma are variable with 2 major common clinical presentations. The first is an asthmatic crisis (“status asthmaticus”) and the second is the chronic clinical presentation of cough and increased breathing effort. There are gradations in the severity and frequency of clinical signs. Cats in status asthmaticus present with open mouth breathing, tachypnea, and increased abdominal effort (“push”) on exhalation. Signs in cats with chronic clinical signs can go unnoticed and untreated by the owner for a long period of time, allowing progression of pathologic changes. It is estimated that 10% to 15% of cats present for vomiting or paroxysmal hacking and coughing[4,7] rather than respiratory distress. Complaints of hacking up hairballs mimicking cough can inadvertently lead to gastrointestinal, not respiratory workups, making identification of a chronic asthmatic patient more challenging.

Classic physical examination findings include cough, expiratory wheeze, and tachypnea.[3–5] Some cats lack abnormalities; however, it is often easy to elicit a cough with gentle tracheal palpation. Aside from these findings, the physical examination is relatively nonspecific, making it important to combine physical examination findings with historical information and results of diagnostic tests to reach a diagnosis of asthma.

DIFFERENTIAL DIAGNOSES

Because there is no single test to diagnose feline asthma definitively, it is important to rule out other diseases that may mimic clinicopathologic features of asthma. Many of

these can be relatively easily differentiated using diagnostics such as thoracic radiographs; others warrant more in-depth discussion given their remarkably similar clinical presentations and radiographic findings compared with allergic asthma.

Chronic Bronchitis

Chronic bronchitis is common in cats and shares many clinical features with asthma such as chronic cough. It is thought to arise secondary to a previous airway insult such as respiratory infections or inhaled irritants. A previous airway insult leads to permanent damage to the airways and results in many of the same historical, physical examination, and radiographic features of asthma. Although cats with either disorder can have a bronchial pattern on thoracic radiographs, cats with asthma have bronchoconstriction in response to inhaled aeroallergen or nonspecific stimulation by inhaled irritants, which results in "air-trapping" that can be visualized on thoracic radiographs as hyperlucent lung fields and displacement of the diaphragm caudally. This should be at least partially reversible with the use of bronchodilators in asthmatic cats. Cats with chronic bronchitis do not have spontaneous bronchoconstriction, although they can have fixed airflow limitation secondary to cellular infiltrates or remodeling changes. Both disorders have differences in cellular infiltrates identified on bronchoalveolar lavage fluid (BALF) cytology with some overlap. Feline allergic asthma is primarily characterized by the presence of eosinophilic inflammation; thus, there should be a predominance ($\geq$17% eosinophils) identified in the BALF.[9] Chronic bronchitis should result in primarily nondegenerate neutrophilic inflammation in BALF. Despite this, there is not always a clear-cut distinction based on BALF as chronic asthma may cause damage to the airways, resulting in some neutrophilic inflammation.[7]

Aelurostrongylosis

Several pulmonary parasitic diseases, including *Aelurostrongylus abstrusus*, can result in similar clinical findings to those seen in asthma, including eosinophilic airway inflammation. *Aelurostrongylus* is a metastrongyloid nematode that infects cats through ingestion of snails, slugs, or paratenic hosts. Radiographically, bronchial to bronchointerstitial lung patterns are typically noted. Although airway eosinophilia is seen with this parasite and with allergic asthma, *Aelurostrongylus* infection can be differentiated by the presence of larvae on BALF cytology or fecal Baermann examination.[10] Because the lack of larvae in these samples does not exclude a diagnosis of *Aelurostrongylus*, empiric treatment with fenbendazole is recommended to more confidently rule out this disorder.

Heartworm Associated Respiratory Disease

Infection with *Dirofilaria immitis* has been proposed to result in heartworm associated respiratory disease (HARD). A preliminary study suggested that death of immature L5 larvae in pulmonary arteries triggers eosinophilic inflammation in the surrounding airways and pulmonary parenchyma.[11] Thus, the presence of adult heartworms might not be necessary for this disease to occur if it is mediated primarily by the larval stage. Diagnostics such as heartworm antigen tests or echocardiography to identify adult heartworms would not not useful in ruling out HARD. HARD should be considered in any cat in an endemic region with appropriate clinicopathologic features and a positive heartworm antibody test that is not receiving heartworm-preventive medication.[12] In addition, there is evidence to suggest that the heartworm endosymbiont, *Wolhbachia*, could contribute to bronchial hyperreactivity in cats with HARD.[13] Thus, it might be useful to treat cats suspected to be affected with HARD with a combination of

selamectin to prevent development of larvae beyond the L4 stage as well as doxycycline to eliminate *Wolhbachia*.

Toxocariasis

Toxocara cati infection is relatively common in the pet cat population. Experimentally, pulmonary and transtracheal migration induces pulmonary and vascular disease in affected cats.[14,15] Experimental *T cati* infection also induces bronchointerstitial lesions on thoracic radiographs and causes BALF eosinophilia; however, cats with *T cati* were clinically asymptomatic and did not seem to have airway hyperresponsiveness, a defining feature of asthma.[16] The role of *T cati* as a differential for spontaneous feline asthma is unclear because airway lesions may be incidental; however, this deserves further study.

Infectious Airway Disease

Airway infection or pneumonia in the cat can result in similar presenting complaints and radiographic findings to those of cats with asthma. See Chapter 7 in this edition for further details. (It refers to the chapter "on bacterial pneumonia" by Jonathan Dear).

DIAGNOSTICS

Diagnosis of feline asthma is based on a combination of appropriate clinical signs and physical examination findings as well as diagnostic testing.

Clinicopathologic Findings

In general, clinicopathologic abnormalities of cats with asthma are nonspecific. Complete blood cell counts have revealed peripheral eosinophilia in 17% to 46% of cases,[3–5,7] but this does not correlate with the degree of airway eosinophilia.[4,5,7] There are no specific serum biochemical or urinalysis abnormalities associated with feline asthma.

Thoracic Imaging

Common findings on thoracic radiography in asthmatic cats include a bronchial or bronchointerstitial pattern.[3–7] Collapse of a lung lobe, particularly the right middle lung lobe, presumably secondary to mucus trapping and atelectasis, can also occur in a minority of cats.[3,6] Lack of radiographic abnormalities does not rule out feline asthma because radiographs can be normal in up to 23% of cases.[3] In addition, as mentioned previously, other diseases can result in similar radiographic findings.

Computed tomography (CT) is used in the evaluation of human asthmatic patients.[17–19] Thoracic CT of cats with lower airway disease can identify abnormalities such as bronchial wall thickening, patchy alveolar patterns, and bronchiectasis[20]; however, these findings have not been compared among cats with different forms of lower airway disease. Thoracic CT likely would identify subtle lesions in cats that would not be appreciated on survey radiographs (**Fig. 1**). CT can be performed in cats using a plexiglass chamber allowing acquisition of images without chemical or manual restraint.[21] This provides an important benefit in cats with respiratory distress unable to tolerate the stress of being restrained for radiography. Preliminary studies suggest CT is capable of discriminating differences in lung attenuation and bronchial wall thickening in cats with experimentally induced asthma compared with healthy research cats.[22] Further study is needed to determine the role of thoracic CT in pet cats with asthma.

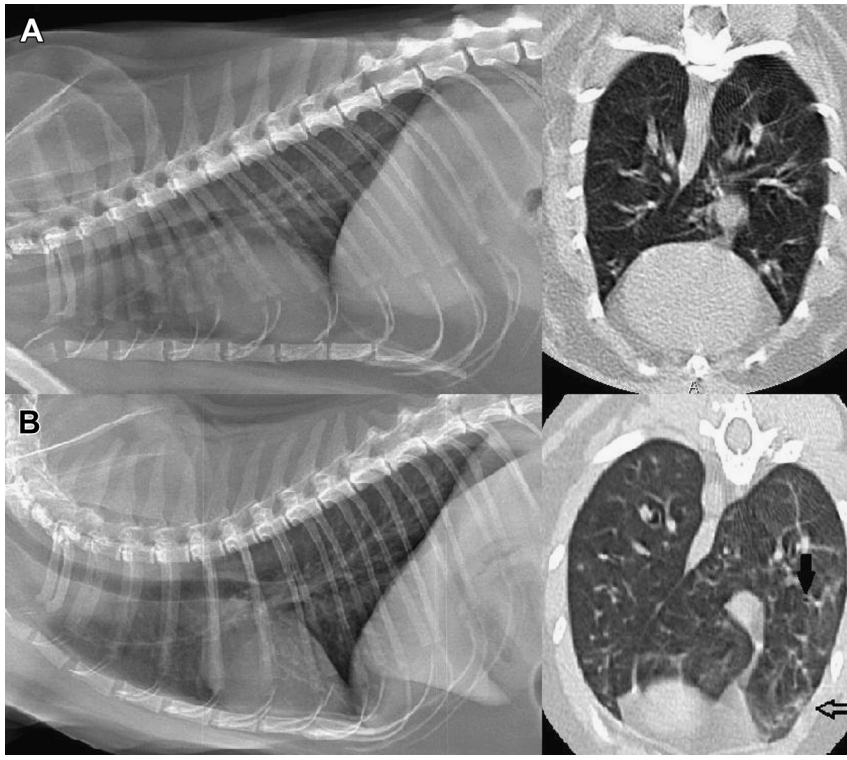

Fig. 1. Representative right lateral thoracic radiographic and computed tomographic (CT) images of 2 awake cats with naturally occurring asthma. CT images were obtained with the cats positioned in a restraining device without the use of anesthetics. The lateral thoracic radiograph of both demonstrates a moderate, diffuse bronchointerstitial lung pattern. On the thoracic CT image of cat (*A*), there is minimal bronchial wall thickening. On the thoracic CT image of cat (*B*), there is prominent bronchial wall thickening (*filled arrow*). In addition, there is a ground-glass appearance to the pulmonary parenchyma particularly in the right lateral lung fields (*open arrow*) with a slight haziness of the lung parenchyma and vasculature from motion artifact. Overall, the CT scan of cat B has increased lung attenuation, whereas cat A has less opaque lung parenchyma despite cat A's lung field being less aerated than cat B, highlighting the benefits of CT compared with thoracic radiography in assessing the severity of structural changes of the airways and pulmonary parenchyma. (*Courtesy of* Isabelle Masseau, DVM, PhD, DACVR, Columbia, MO.)

Bronchoscopy and Bronchoalveolar Lavage Cytology

Bronchoscopy is useful for visual inspection and collection of samples from cats with lower airway disease. Lesions include mucus accumulation, mucosal hyperemia, epithelial irregularities, airway collapse and stenosis, as well as bronchiectasis, although unfortunately, these abnormalities do not discriminate between asthma and other forms of lower respiratory disease.[23] Bronchoalveolar lavage fluid samples for cytologic examination can be collected using bronchoscopy or via a blind technique. Eosinophilic inflammation is noted on BALF cytology of asthmatic cats; however, what constitutes normal cellular percentages in BALF fluid is controversial. Reported "normal" eosinophil percentages in cats have ranged from 0% to 83%.[24–27] In many of these studies, healthy cats have been defined as those free of

clinical signs. In human asthmatics, airway inflammation can be present despite the absence of overt symptoms,[28,29] and subclinical inflammation has also been documented in pet cats.[30] Thus, it is possible that some healthy control cats in studies of feline BALF cytology were not appropriate and a cutoff of $\geq$17% BALF eosinophils in pet cats has been proposed as abnormal for some studies.[9,24] Finally, as discussed previously, parasitic diseases result in airway eosinophilia; thus, eosinophilic inflammation is not specific to feline asthma. The findings of eosinophilic airway inflammation should be interpreted in conjunction with clinical signs and diagnostic testing.

Adjunctive Testing

In addition to routine blood testing, thoracic imaging, bronchoscopic examination, and BALF cytology, other diagnostics are used to support a diagnosis of feline asthma and eliminate alternative diagnoses.

Culture of BALF, regardless of whether organisms are detected on cytology, is warranted. In addition, if cultures of *Mycoplasma spp* cannot be performed, PCR should be considered because this is one of the more common opportunistic pathogens in feline lower airway disease.[31] Cats with airway eosinophilia should have a heartworm antibody/antigen test to evaluate for HARD and a fecal floatation and Baermann examination for *T cati* and *A abstrusus*, respectively. It is important to realize that normal results do not rule these diseases out completely.

Allergy Testing

Allergy testing by intradermal skin testing or serum allergen-specific IgE can be used to identify sensitizing allergens implicated in disease, although these are not commonly used in pet cats with asthma. With appropriate identification, allergen avoidance or, in the future, allergen-specific immunotherapy might be used to reduce or eliminate clinical signs in affected cats (see Treatment section).

Pulmonary Function Testing

An important clinical feature of asthma is airflow limitation that is at least partially reversible with bronchodilators. In humans, spirometry is used to gauge lung function. Spirometry requires patient compliance to exhale through a mouthpiece forcefully, making it unsuitable for cats. Alternative pulmonary function testing in cats includes tidal breathing flow-volume loops using a tight fitting face mask, forced expiratory flow-volume curves using a thoracic compression technique, barometric whole body plethysmography (BWBP), and ventilator-acquired lung mechanics.[32–36] Pulmonary function testing is reviewed in chapter 9 of this edition and refers to the chapter by Balakrishnan and Lesley King.

There has been growing interest in using BWBP as a noninvasive test to differentiate between feline asthma and chronic bronchitis. Bronchoprovocation using BWBP discriminates normal cats from cats with lower airway disease,[37] although it is important to understand that BWBP is influenced by the respiratory cycle and does not directly measure airway resistance.[38] Cats with asthma were more likely to demonstrate airflow limitation in response to challenge with an indirect bronchoprovocant than cats with chronic bronchitis.[37] In addition, there was a correlation between the degree and type of airway inflammation and airflow limitation measured by BWBP in spontaneous feline bronchial disease.[39] Namely, cats with airway eosinophilia demonstrated airway hyperresponsiveness at lower doses of the bronchoprovocant than cats with airway neutrophilia. The gold standard technique to measure airway resistance is direct pulmonary mechanics. In experimental feline asthma, ventilator-acquired pulmonary mechanics allow direct and specific calculations of airway resistance and

have particular value in assessing effects of therapy on airflow limitation.[22,32,40] Additional studies are needed to determine how well these 2 types of pulmonary function tests correlate.[37,40,41]

TREATMENT

The mainstay of therapy for feline asthma consists of lifelong steroids with or without bronchodilators. Unfortunately, these medications are not effective in all cats, can be associated with adverse effects, and are contraindicated in some cats with concurrent diseases. Therapies that might help to reverse the underlying immunopathology of asthma or could be used as adjuncts in refractory asthma are being investigated in experimental feline asthma models. Although these models are important in identifying therapies that may be effective in asthma, they might not accurately reflect all aspects of spontaneous asthma. Thus, it is critical that studies are repeated in pet cats with asthma.

Traditional Therapies

Glucocorticoids

Steroids are potent anti-inflammatories that have long been used for the treatment of feline asthma. They are most often administered orally in the form of prednisolone; however, inhaled therapy using a spacing chamber (Aerokat; Trudell Medical International, Ontario, Canada) is becoming more commonplace. There are no prospective, controlled studies evaluating the use of glucocorticoids in cats with spontaneous asthma; however, glucocorticoids are considered to be an effective therapy in most cats. Many retrospective studies have reported a beneficial response to glucocorticoids.[3–6] Unfortunately, therapeutic response in these studies is often based on improvement in clinical signs without documenting improvement in airway inflammation or hyperresponsiveness. Given the waxing and waning nature of the clinical signs of asthma, it is difficult to assess the true effectiveness of therapy based on clinical signs alone.

In experimental feline asthma, both oral prednisone (10 mg/d) and inhaled flunisolide (500 μg/d) significantly decreased airway eosinophilia compared with placebo.[42] Using a different experimental feline asthma model, fluticasone propionate with salmeterol (500 μg fluticasone/50 μg salmeterol twice daily) was as effective as oral prednisolone (2 mg/d) at reducing airway inflammation in acute asthma.[43] In a follow-up study by the same group, oral prednisolone (2 mg/d) was compared with inhaled salmeterol (50 μg twice a day) over a 4-day period.[44] Only oral prednisolone was capable of eliminating the late phase asthmatic reaction in response to inhaled allergen.[44] Although an effective dose in pet cats has not been established, comparison of varying doses of inhaled fluticasone (44, 110, or 220 μg twice daily) suggests all are equipotent in controlling airway eosinophilia in experimental asthma.[45]

Bronchodilators

Bronchodilators are critical to reduce bronchoconstriction in acute asthma attacks. However, they should not be used for monotherapy because they fail to control the airway inflammation that exacerbates airway hyperresponsiveness.[8] Several different types of bronchodilators have been assessed, mostly in experimentally asthmatic cats, including methylxanthines,[46,47] short-acting and long-acting β-2 agonists (SABA[5,46,48–50] and LABA,[44,46,48] respectively) and anticholinergics.[46,48,49] When using a compound that directly constricts smooth muscle (ie, carbachol), inhalation of a bronchodilator via a metered dose inhaler and nebulization were equally effective in blunting airway hyperresponsiveness.[48] Also, SABA were more potent than LABA and with combination SABA/anticholinergic bronchodilator therapy, synergism was

noted.[48] Interestingly, after specific allergen bronchoprovocation, bronchodilators did not improve time to recovery compared with no treatment.[49] For this reason, the authors prefer use of the injectable bronchodilator terbutaline in pet cats with life-threatening status asthmaticus. Although SABA are critical in treating life-threatening bronchoconstriction, overuse by inhalation has been associated with increased risk of death in human asthmatics.[51] Inhalant albuterol is a racemic mixture consisting of the R-enantiomer, which possesses bronchodilatory properties, and the S-enantiomer (initially thought inert), which promotes bronchospasm and is pro-inflammatory.[52] With repeated use, the S-enantiomer preferentially accumulates in the lung because of slower metabolism/clearance, enhancing bronchoconstrictive and proinflammatory effects.[53] Chronic use (twice daily for 2 weeks) in healthy cats induced de novo neutrophilic airway inflammation; in experimentally asthmatic cats, esoinophilic airway inflammation was exacerbated.[52] This exacerbation indicates that although inhaled albuterol can be an important therapy for acute bronchoconstriction (especially as at-home treatment), it should not be used in the daily management of asthmatic cats. A single isomer form of R-albuterol (levalbuterol) is available, is not associated with negative adverse effects, and could be considered an option for chronic therapy.

Experimental Therapies

Allergen-specific immunotherapy

No therapy to date reverses the underlying immunopathology associated with spontaneous feline allergic asthma. Allergen-specific immunotherapy has emerged as a potentially curative therapy in human medicine as it is proposed to reverse the T helper 2-mediated allergic response by inducing immunologic tolerance to allergen. Several different protocols have been investigated in an experimental model of feline asthma using an abbreviated or "rush" administration (rush immunotherapy, RIT) and have successfully diminished airway eosinophilia.[54–56] Before pet cats with asthma can be treated, allergens implicated in airway sensitization must be identified. Using cats experimentally sensitized to Bermuda grass or house dust mite, the sensitivity and specificity of intradermal skin testing and 2 different forms of serum allergen testing using either an FcεR1α-based ELISA or an enzymoimmunometric assay were investigated.[57] The sensitivity of the IDST was greater than the FcεR1α-based ELISA (ie, better screening test); however, both were specific (ie, suitable for allergen selection for RIT). Disappointingly, the enzymoimmunometric assay produced unreliable results including failure to detect allergen-specific IgE and identification of allergens to which the cats had not been sensitized. Future studies should be performed to evaluate more rigorously the accuracy of diagnostic laboratories offering allergen-specific IgE testing. To determine the importance of closely matched allergens for use in RIT, an additional study was performed in experimentally asthmatic cats.[58] Use of allergens not implicated in sensitization or use of only 1 of 2 sensitizing allergens in RIT still led to reductions in airway eosinophilia. However, only closely matched allergens had the potential to induce an immunologic cure by induction of tolerance, which could potentially allow discontinuation of therapy with permanent benefit.

Omega-3 fatty acids/neutraceuticals

Omega-3 Polyunsaturated fatty acids are anti-inflammatory due to reduction of arachadonic acid in cell membranes available for production of inflammatory eicosanoids.[59] The use of dietary ω-3 polyunsaturated fatty acids in combination with the antioxidant, luteolin, has been evaluated in experimental feline asthma.[60] This treatment failed to

resolve airway eosinophilia, but diminished airway hyperresponsiveness as assessed by BWBP. Although clearly unsuitable as monotherapy, additional studies in pet cats with asthma might help determine if they could be used as adjunctive therapy.

Inhaled lidocaine

Lidocaine has received interest in human medicine as a potential treatment of severe asthma[61–63] and has been investigated in an experimental feline asthma model.[64] In the latter study, nebulized lidocaine (2 mg/kg q8h) was administered to healthy and experimentally asthmatic cats for 2 weeks. Lidocaine decreased airway hyperresponsiveness without decreasing airway eosinophilia. Importantly, no adverse effects were noted in the cats despite the known sensitivity of cats to injectable lidocaine. Further study is needed to determine if lidocaine might be useful to treat airflow limitation in spontaneous feline asthma.

Tyrosine kinase inhibitors

Blockade of key cell signaling pathways involved in the immunopathogenesis of asthma could lead to novel avenues of treatment. Both receptor and nonreceptor tyrosine kinase inhibitors (TKIs) have potential in this regard. For example, stem cell factor, the growth factor for the c-kit receptor, is associated with proliferation and activation of both mast cells and eosinophils[65] and, in experimental feline asthma, these can be inhibited with TKIs such as masitinib.[32] Cats receiving masitinib (50 mg/d by mouth) showed decreases in BALF eosinophilia and lung compliance as measured by ventilator-acquired pulmonary mechanics. Unfortunately, side effects were dose-limiting. Inhibition of the janus kinase cytokine signaling pathway by a nonreceptor TKI was also evaluated in feline asthma.[66] In a preliminary study, cats showed reduction of airway eosinophilia without a significant effect on airway hyperresponsiveness.

Stem cells

Stem cells have been studied for the treatment of a variety of respiratory disorders including asthma. Murine asthma models have demonstrated that stem cells can reduce airway eosinophilia, airway hyperresponsiveness, and airway remodeling.[67–70] Early data suggest that the most beneficial effects of intravenously administered allogeneic feline adipose-derived stem cells in experimental asthma might be amelioriation of airway remodeling as assessed by thoracic CT scans.[71] These stem cells are not the same as commercially available products, and further studies are needed before stem cells are recommended for feline asthma.

Ineffective Therapies

Leukotriene antagonists are part of the arsenal of medications used for treatment of human asthmatics. Unfortunately cysteinyl leukotrienes do not seem to be important mediators of feline asthma[72,73] and a clinical trial with the leukotriene antagonist, zafirlukast, failed to reduce airway eosinophilia or hyperresponsiveness in experimental feline asthma.[42] Serotonin is a preformed mediator in mast cells and is thought to be important in mediating bronchoconstriction in response to allergen exposure.[73,74] Cyproheptadine, a nonspecific serotonin antagonist, at a low dose (2 mg q12h by mouth) failed to significantly reduce airway reactivity and airway inflammation in experimentally asthmatic cats.[42] A subsequent study[75] evaluated a higher dose of cyproheptadine (8 mg q12h by mouth) based on a pharmacokinetic study, suggesting cats may require substantially higher doses than what has been traditionally recommended to reach therapeutic concentrations.[76] Even at this dose, cyproheptadine was ineffective at reducing airway eosinophilia. Because hyperresponsiveness was not evaluated in this study, it is uncertain if the higher dose could alleviate airflow

limitation. Although not advocated for monotherapy, the higher dose deserves further study to evaluate its bronchodilatory properties. Histamine, like serotonin, is present in the granules of mast cells and could have similar effects on airway reactivity.[74,77–80] A study investigating the second-generation antihistamine, cetirizine (5 mg q12h by mouth), found that airway eosinophilia was not significantly diminished.[75] The effect of cetirizine on airway hyperresponsiveness is currently not known and further study is needed before this therapy can be recommended.

A salivary tripeptide (feG-COOH) identified as a modulator of the immune response reduced allergen-induced airway inflammation in other animal models of asthma.[81,82] Chronic administration of feG-COOH (1 mg/kg/d for 2 wk) did not blunt airway eosinophilia compared with placebo in experimental feline asthma and cannot be advocated.[83] Oral doxycycline (5 mg/kg twice daily) failed to blunt airway eosinophilia or hyperresponsiveness.[44] N-acetylcysteine is a mucolytic with antioxidant properties that could have a benefit in asthma; however, nebulized delivery in humans is known to induce bronchospasm. Similarly, in experimentally asthmatic cats, nebulization of N-acetylcysteine increased baseline airway resistance by an average of approximately 150% and should not be administered by this route.[40]

MONITORING

Traditionally, titration of therapy in asthmatic cats relies on observation of reduction in clinical signs. However, clinical signs of asthma can wax and wane, making it difficult to determine if the reduction in clinical signs is related to a true effect of the medication. Recently, a retrospective study investigated the presence of inflammation on BALF cytology after initial treatment with high-dose glucocorticoids and found that despite cats having no clinical signs of asthma at the time of sampling, many had subclinical inflammation noted on BALF cytology.[30] Importantly, unchecked airway inflammation can lead to irreversible remodeling resulting in a decline in lung function.[84–86] Until a less invasive diagnostic test is developed, repeated analysis of BALF cytology could be necessary before making alterations in treatment protocols in asthmatic cats.

SUMMARY

Much work must be done to define feline asthma better and discriminate it from other lower airway diseases. Importantly, accurately identifying asthmatics will help more appropriately select candidates for targeted therapies acting along the allergic cascade. Although many experimental therapies are being investigated in feline asthma, work is still needed to determine if these will be beneficial in our pet cat population.

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