Evidence of Lung Remodeling as Assessed by Computed Tomography in Experimental and Spontaneous Feline Asthma

Alina Banuelos,1 Isabelle Masseau,1,2 Carol Reiner01
Department of Veterinary Medicine and Surgery and the Comparative Internal Medicine Laboratory1, Veterinary Pathobiology2 College of Veterinary Medicine, University of Missouri

INTRODUCTION

Allergic asthma, a remarkably similar disease in humans and cats, has been on the rise in both species in recent years. Airway remodeling (permanent architectural changes in the lung) is a prominent feature of the disease for which there are no effective treatments. While rodent models of asthma are important to help dissect mechanistic information, rodents do not spontaneously develop asthma and have important differences in anatomy, physiology and immunology compared with humans. A more clinically relevant model of allergic asthma has been developed in cats, the only animal species to spontaneously develop a syndrome of asthma with all the major features of the human disease. This feline model has allowed for tightly controlled experiments, but is still understood to be a model and susceptible to limitations. Pet cats with spontaneous asthma also hold potential to be studied, but remodeling in particular is not well characterized. While lung biopsy is the definitive means to assess for remodeling, it is invasive; thus, computed tomography (CT) has received interest as a non-invasive surrogate diagnostic. The purpose of this study was to compare indices of airway remodeling between cats with experimentally induced and spontaneous asthma and healthy unaffected cats using CT.

HYPOTHESIS

We hypothesized experimental and spontaneous feline asthma would have similar remodeling changes noted on CT and would be significantly different from healthy cats.

METHODS

Animals—Healthy research cats (n=5), research cats with experimental asthma (5), and pet cats with spontaneous asthma (5) were studied. Bermuda grass allergen (BGA) was used to induce and maintain an experimental asthma phenotype for 9 months prior to study. Asthmatic pet cats were patients at the VMTH, University of Missouri.

Computed tomographic (CT) scans—Scans were performed on each cat using a multidetector CT scanner (Aquilion 64, Toshiba Merican Medical Systems, Tustin, CA) with a positioning/restraining device (Vet Mouse Trap) that avoids the need for anesthesia. Images of the entire lung field were obtained and consisted of 1-mm thick contiguous transverse images. Total volume and mean and standard deviation of the lung attenuation for each cat were extracted from the CT scans using the 3D Slicer software program (3D Slicer.org). Consecutive 1-mm slices from the CT scans were chosen for analysis of mean tracheal lumen attenuation. From each slice, attenuation, in Hounsfield units (HU), was measured starting from the beginning of the trachea and ending just prior to the tracheal bifurcation. Mean and standard deviation of the lung attenuation (an index of variability in homogeneity of lesions) were normalized to the tracheal lumen attenuation for each cat. Total volume was normalized to the body weight (kg) for each cat.

Statistical analysis—Data were analyzed using Sigma Plot (Systat Software, Inc, San Jose, CA). Normally distributed data were analyzed using a One Way Analysis of Variance (ANOVA) and post-hoc testing performed using the Holm-Sidak method. Non-normally distributed data were analyzed using the Kruskal Wallace One Way Analysis of Variance on Ranks and post-hoc testing performed using a Tukey test. P<0.10 was considered significant.

RESULTS

Figure 2. CT scans of a healthy cat (A), experimentally induced asthmatic cat (B), and spontaneously asthmatic pet cat (C) taken at the level of the caudal and accessory lung lobes. Healthy cat lungs are darker and much more homogeneous when compared to the experimentally induced and spontaneously asthmatic cats. Both experimentally induced and spontaneously asthmatic cats had an increase lung attenuation, bronchial thickening, and heterogeneity of the lung parenchyma.

Figure 1A. Image is of an awake cat undergoing a CT scan in the restraining device (Vet Mouse Trap) that eliminates the need for sedation. Figure 1B. Histogram of total lung attenuation obtained after extraction of the lung from the CT scan using 3D Slicer software program.

CONCLUSION

In conclusion, this small pilot study showed one CT-derived measure of airway remodeling (lung attenuation) was similar in experimental and spontaneous asthma and was significantly different from healthy cats. While awake and unrestrained CTs have the advantage of not requiring anesthesia, hypoinflation and motion artifact preclude analysis of other parameters such as bronchial wall thickness that could be obtained from anesthetized CTs. Further studies using CT may be useful in experimental and spontaneous feline asthma “models” to investigate pathogenesis and new therapies targeting remodeling.

ACKNOWLEDGMENTS

Stipend was provided by a grant from Merial, a Sonofi company and project supplies were provided by a Richard Wallace Research Incentive grant.