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

Alina Banuelos,[1] Isabelle Masseau,[1,2] Carol Reinero[1]

Department of Veterinary Medicine and Surgery and the Comparative Internal Medicine Laboratory[1], Veterinary Pathobiology[2] 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 1mm 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 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.

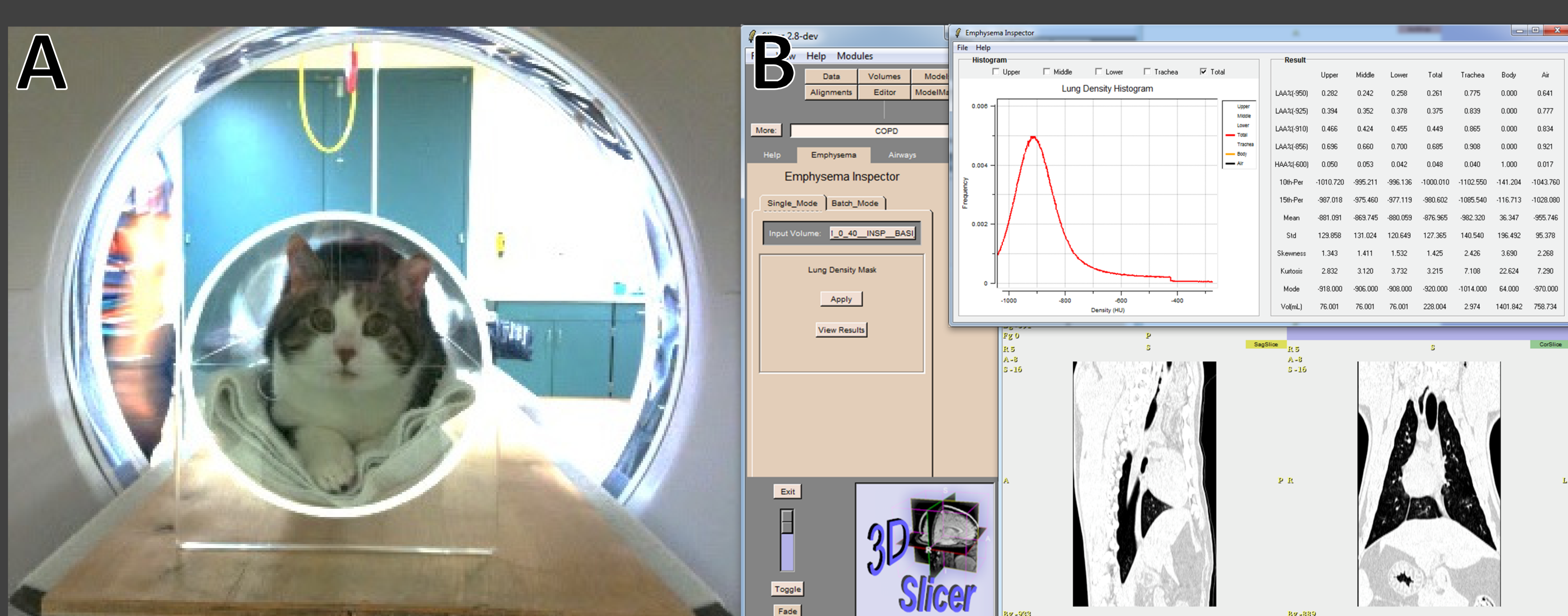

Figure 1A. Image is of an awake cat undergoing a CT scan in the restraining device (Vet Mouse Trap) that eliminates the need for sedation. Figure 1B. Histogram of total lung attenuation obtained after extraction of the lung from the CT scan using 3D Slicer software program.

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 homogenous 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.

Animals:
Signalment, body weight and BAL cytology of research cats—All research cats were domestic shorthairs and intact males; healthy cats were 2 years of age and asthmatic cats were 1 year old. The group mean±SD body weight was 4.54±1.02 kg for healthy cats and 5.36±0.95 kg for asthmatic cats. Healthy research cats had group mean±SD % bronchoalveolar lavage (BAL) eosinophils of 7±5%; experimentally asthmatic cats had 58±12%.

Clinicopathologic features of spontaneously asthmatic pet cats--Five spontaneously asthmatic pet cats with veterinary diagnosed asthma were studied. Breeds included DSH (n=2), Ocicat (1), Cornish Rex (1), and Siamese (1). Four cats were female (3 spayed, 1 intact) and one cat was an intact male. Mean age was 8.2 years (range, 4 to 14 years) and group mean±SD body weight was 5.46±1.01 kg. Clinical signs included chronic cough (n=5) and increased respiratory effort (n=2). Thoracic radiographs revealed a bronchointerstitial pattern (n=5), alveolar infiltrate (1), and cardiomegaly (2). The group mean ±SD % BAL eosinophils was 55.8±26%.

CT parameters:
Mean lung attenuation--There was a significant difference in mean lung attenuation between the three groups of cats (group mean±SEM: healthy cats -865.536±34.4 HU; experimentally asthmatic cats -738.152±20.1 HU; pet asthmatic cats-769.886 ± 35.6 HU; P=0.032). Post-hoc testing demonstrated that healthy cats had significantly lower mean lung attenuation than experimentally asthmatic and spontaneously asthmatic cats (P=0.038 and P=0.095, respectively).

Standard deviation of lung attenuation (degree of heterogeneity of attenuation)—There was no significant difference in degree of heterogeneity of attenuation between the groups of cats (group mean±SEM: healthy cats 130.182± 12.627 HU; experimentally asthmatic cats 145.338± 1.637 HU; pet asthmatic cats 142.987± 5.273 HU; P=0.380).

Total lung volume—There was no significance between the median lung volume between groups (median {IQR}: healthy cats, 50.6 {26.2, 93.7}; experimentally asthmatic cats, 37.9 {34.1, 49.4}; pet asthmatic cats, 25.5 {15.2, 41.7}; P=0.221).

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 experimentally and spontaneous feline asthma “models” to investigate pathogenesis and new therapies targeting remodeling.

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