Title: Computed Tomographic Findings in 15 Dogs with Eosinophilic Bronchopneumopathy

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ABSTRACT

Eosinophilic bronchopneumopathy (EBP) is a disease characterized by the infiltration of the lung and bronchial mucosa by eosinophils.[1] The aim of this study was to describe the computed tomographic (CT) findings in dogs with confirmed diagnosis of EBP. CT scans of 15 dogs with confirmed diagnosis of EBP were evaluated retrospectively by 2 boarded radiologists who reached a consensus. Abnormalities were identified in 14/15 (93%) dogs, including pulmonary parenchymal abnormalities in 14/15 (93%) dogs, bronchial wall thickening in 13 (87%) dogs, which was considered marked in 8 (53%), plugging of the bronchial lumen by mucus/debris in 11 (73%) dogs, bronchiectasis in 9 (60%) dogs, and pulmonary nodules in 5/15 (33%) dogs. Lesions associated with EBP are variable and heterogeneous, and encompass a wider variety of CT features than reported previously. CT images were abnormal in the majority of affected dogs, hence CT is a useful modality to characterise the nature and distribution of thoracic lesions in dogs with EBP.

Introduction

Eosinophilic bronchopneumopathy (EBP) is a canine pulmonary disease characterized by the infiltration of the lung and bronchial mucosa by eosinophils.[1] Nomenclature of eosinophilic lung disorders in dogs is inconsistent[2] with this condition also described in the veterinary literature as pulmonary infiltration with eosinophils[3], pulmonary eosinophilia[4] and eosinophilic pneumonia[2-4]. The cause of canine EBP remains unclear, although hypersensitivity to aeroallergens is suspected.[1] In most affected dogs the inciting cause is not identified.[1]

EBP occurs most often in young adult dogs, and more commonly in females than males.[1, 2] A breed predisposition for Siberian Huskies and Alaskan Malamutes has been reported[1], but dogs of many breeds may be affected[2]. Cough is the most consistent clinical sign, but gagging, retching, respiratory effort and non-respiratory signs, such as weight loss, may also be present.[1, 2] Diagnosis of EBP is based on diagnostic imaging and bronchoscopic findings, demonstration of eosinophilic infiltration by cytology of bronchoalveolar lavage (BAL) or histopathologic examination of bronchial biopsies, and through exclusion of other causes of eosinophilic infiltration of the lower airways (e.g. parasitic disease).[2,5]

There have been few reports of the imaging findings in dogs with EBP. The radiographic signs in a series of 23 dogs with EBP included a moderate to severe diffuse bronchointerstitial lung pattern (65%), alveolar infiltration (40%), bronchiectasis (26%), and peribronchial cuffing (21%).[1] A case report of the computed tomographic (CT) findings in a dog with EBP described diffuse, severe cylindrical bronchiectasis with multifocal, complete to partially obstructive, accumulations of fluid or tissue.[6] A recent report of CT findings in 5 dogs with EBP also emphasized diffuse, severe cylindrical bronchiectasis and bronchial obstruction by fluid or tissue.[7] The aim of the present study was to describe the CT findings in a larger series of dogs with confirmed diagnosis of EBP.

Materials and Methods

The clinical archives of the Small Animal Teaching Hospital, University of Liverpool (SATH) and The Royal Veterinary College, University of London (RVC) were searched from 2007 to March

2013 and from 2005 to March 2013, respectively, for dogs that had thoracic CT scan and a diagnosis of EBP within seven days of imaging.

Diagnosis of EBP was based on finding eosinophilic infiltration in cytologic or histologic samples obtained from the airways, and exclusion of concurrent parasitism by BAL, faecal analysis for *Angiostronglyus vasorum*, or appropriate anthelmintic therapy prior to diagnosis. A percentage of eosinophils in the cytologic preparation greater than 19% of the total nucleated cells was considered consistent with eosinophilic infiltration.[8]

CT scans were examined retrospectively by two boarded radiologists (FMc and CRL). All images were reviewed in a single sitting using a computer workstation with DICOM viewer software (OsiriX Pixmeo, Geneva, Switzerland (version 4.1.1 64-bit)). Both lung and soft tissue reconstructions were reviewed. Adjustments to image window width and level, multiplanar reconstructions, and maximum and minimum intensity slab projections were done as considered necessary for examination of each case. Observers recorded their observations about each case directly into a spreadsheet that prompted entries for a range of imaging signs that had been formulated and agreed by the observers in advance based on review of a previous study[9]. Observers reached agreement by discussion about the description of abnormalities present in each case.

The general distribution of the lung lesions was classified as generalised, lobar, focal or multifocal. The lobar distribution was classified as perihilar, peripheral, peribronchial or diffuse. The lung patterns were classified as ground-glass, septal, nodular, crazy paving or consolidation. A ground-glass lung pattern was characterized by a hazy increase in the lung attenuation without obscuration of the underlying pulmonary vessels. A septal pattern was defined by thickening of interlobular septae. The nodular pattern was divided in three categories according with the diameter of the nodular lesions (small <10mm, large 10- 30 mm, mass > 30mm). A “crazy-paving” pattern was classified as ground-glass opacity with superimposition of a reticular pattern.[10] Consolidation was defined as increased lung attenuation that obliterated pulmonary vessels, with or without air bronchograms. The thickness of the bronchial walls was subjectively evaluated and classified as normal, slightly thickened or markedly thickened. The presence of plugging of the bronchial lumen by mucus/debris and the presence of consolidation of the plugged bronchi was recorded. The presence of bronchiectasis was identified by

lack of tapering of the bronchial lumen towards the lung periphery, visible bronchi within 1cm of the lung margin or a bronchoarterial (BA) ratio >2.0. The distribution of bronchiectasis was classified as focal or generalized, and the type as cylindrical, saccular or varicose. Cylindrical bronchiectasis was characterized by dilatation of the bronchi without tapering toward the periphery.[11,12] Saccular bronchiectasis referred to airway dilatation that included focal saccular dilatations or cyst-like structures.[11,12] Varicose bronchiectasis was defined as focally dilated bronchial segments interposed between normal.[12,13] The severity of bronchiectasis was classified as slight if the BA ratio was between 2.0-2.4, moderate if between 2.5 and 3.0 and severe if the BA ratio was >3. Pulmonary arteries were assessed subjectively for evidence of enlargement that could indicate pulmonary hypertension. Lymphadenopathy was characterized by a lymph node short axis diameter in transverse images >10mm. Lymphadenopathy was subjectively graded as slight if there was no displacement of the perinodal structures and graded as marked if there was displacement of the perinodal structures. The involved lymph nodes were recorded. Additional findings (presence of tracheal exudate, pleural effusion, pneumothorax, pleural nodules/thickening) were also recorded if present.

Results

Fifteen dogs meet the inclusion criteria. Breeds were Springer Spaniel (n = 3), Labrador retriever (n = 3), crossbreed dogs (n = 2), Irish terrier (n = 2), Siberian Husky (n = 1), German Shorthaired Pointer (n = 1), Sharpei (n = 1), Scottish Terrier (n = 1), and Rottweiler (n = 1). There were nine males (six castrated) and five females (four castrated). Their ages ranged from 7 months to 11 years (mean 4 years). The most frequent clinical sign was chronic cough, which affected 14/15 dogs. Diagnosis of EBP was based on cytology from the bronchioalveolar lavage fluid alone in 11 dogs, cytology from the bronchioalveolar lavage fluid and bronchial brush in 3 dogs, and histology of bronchial biopsies and cytology from the bronchioalveolar lavage fluid in one dog. The Baermann test was performed in all dogs and was negative in each case with no *Angiostrongylus spp*. larvae seen.

Computed tomographic scans were obtained using multidetector scanners (4-slice at SATH (Siemens SOMATOM, Siemens Healthcare Diagnostics, Deerfield, IL) and 16-slice at The RVC (Mx8000 IDT, Philips, Best, The Netherlands) with all dogs positioned in sternal recumbency. Twelve

dogs had CT under general anesthesia and three were sedated. The most commonly used general anesthesia protocol included the premedication with medetomidine (0.002 mg/kg, intravenously) and butorphanol (0.2 mg/kg, intraveneously), induction with intravenous propofol (dose to effect) and volatile maintenance on isoflurane (1.5–2%) in oxygen via an appropriate breathing system. The most common protocol used for sedation included the intravenous administration of medetomidine (0.002–0.003 mg/kg) and butorphanol (0.2 mg).

For dogs under general anesthesia, the CT scan was performed during temporary apnoea induced by hyperventilation in six dogs, and during manual inflation and breath holding in the other six. Breath holding was achieved holding the bag manually at the pressure of approximately 15 cm of water during the scan. Scan parameters differed for individual patients. The most common protocol used consisted of a helical volumetric acquisition using 1.5 mm collimation, pitch 1, 0.5 s rotation time, 150 mA, 120 kVp, and 500 mm acquisition field of view. The reconstruction field of view depended on patient body size (varying between 180 and 250 mm). Reconstructions were most commonly generated with a 3 mm slice thickness using a standard (soft tissue) kernel and 1.5–2 mm slice thickness with a sharp (lung) kernel. Reconstructions with both standard and sharp algorithms were available for review for all dogs. Intravenous iodinated contrast medium (Omnipaque, iohexol, 300 mg I/ml, GE Healthcare AS, Nycoveie 1–2, NO-0401 Oslo, Norway) at the dose of 600 mg iodine/kg body weight was used in 11/15 dogs. The post contrast images were obtained immediately following intravenous contrast bolus injection. In six of these dogs, a pressure injector (Stellant® Sx, Medrad, Newbury, RG14 1JA, UK) was used with contrast agent administrated at 2–3 ml/s, dependant on patient weight. Contrast medium was injected manually in the remaining five dogs.

Computed tomographic images were considered abnormal in 14/15 (93%) dogs (Fig. 1). Pulmonary parenchymal abnormalities were found in 14/15 (93%) dogs and was the most common abnormality found (Figs. 2 and 3). The distribution of the lesions within the lungs was generalized in 7/15 (47%) dogs and multifocal in 6/15 (40%) dogs. A lobar distribution was seen in only one dog. Within affected lung lobes, the most frequent distribution of the lesions was peribronchial, this was seen in 10/15 (67%) dogs. Diffuse and peripheral lobar distribution was seen in 7/15 (47%) and 6/15 (40%) dogs, respectively. A perihilar distribution was not seen in any dog. A ground-glass pattern and

areas of lung consolidation were the most frequent lung patterns, and were observed in 11/15 (73%) and 10/15 (67%) dogs, respectively. A nodular pattern was observed in 5/15 (33%) dogs (Fig. 3). Three of the dogs with lung nodules had only small nodules and one dog had a combination of small and large nodules. One dog had a pulmonary mass (Fig. 4). All dogs with a nodular lung pattern had additional abnormalities including a concomitant lung pattern in 5/5 (100%), bronchial thickening in 4/5 (80%), lymphadenopathy in 4/5 (80%) or plugging of the bronchial lumen in 3/5 (60%) dogs.

Bronchial wall thickening was present in 13/15 (87%) dogs, which was considered marked in 8 (53%) and slight in the remaining 5 (38%) (Fig. 5). Plugging of the bronchial lumen by mucus/debris was noted in 11/15 (73%) dogs (Fig. 6). Bronchiectasis was present in 9/15 (60%) dogs and in all cases was classified as focal (Fig. 7). Bronchiectasis was considered severe in five dogs and moderate in four. Bronchiectasis was classified as cylindrical in six dogs, saccular in one, and a combination of cylindrical and saccular in the remaining two dogs. Intrathoracic lymphadenopathy was observed in 10 dogs (67%) and was classified as slight in seven dogs and marked in three. The tracheobronchial lymph nodes were considered enlarged in five dogs and the cranial mediastinal in one. The remaining four dogs with lymphadenopathy had enlargement of the tracheobronchial and cranial mediastinal lymph nodes. Tracheal exudate was visible in three dogs. One dog had enlarged pulmonary arteries. No other vascular abnormalities were observed. One dog had a small pulmonary bulla and one dog had pleural thickening.

Discussion

A recent report describing the CT features of canine EBP[6] described diffuse, severe cylindrical bronchiectasis with multifocal complete to partially obstructive accumulations of fluid or tissue. The results of the present study were similar with plugging of the bronchial lumen by mucus/debris, bronchiectasis and bronchial wall thickening being observed frequently. It appears that many dogs with EBP have advanced bronchial lesions at the time of diagnosis. In addition, we found a wider variety of CT features than has been previously described including pulmonary parenchymal lesions, some of which appeared nodular.[6] In fact, pulmonary parenchymal lesions were the most frequent finding in the present study (93%) and were typically characterized by generalized areas of ground-glass pattern or consolidation. This high prevalence of pulmonary changes seen on CT is in agreement to a report of

radiological abnormalities in dogs with EBP[1] where pulmonary lesions were visible in all affected dogs. In that study the most frequent lung changes were a mixed broncho-interstitial lung pattern and alveolar infiltration, which are analogous to our findings.

The differential diagnosis for eosinophilic lung diseases in dogs includes eosinophilic pulmonary granulomatosis (EPG) and lungworm infection. EPG is an inflammatory nodular lung disease that shares some features with EBP, such as evidence of pulmonary eosinophilic infiltration and often peripheral eosinophilia.[1] However it is differentiated by more severe clinical signs[1], presence of multiple masses of various sizes that tend to obliterate the normal pulmonary architecture[1,9] and by a poorer prognosis[1,7]. It is uncertain if EPG represents a progressive form of EBP or a different disease.[1] In a recent study, the CT characteristics of dogs with EPG commonly included pulmonary masses and nodules of variable size and areas interstitial and alveolar lung infiltration.7 In that study, all but one large eosinophilic granuloma had a typical honeycomb-like enhancement pattern consisted of multiple hyperattenuating rims delineating central hypoattenuating areas, suggestive of bronchiectatic lung with peripheral enhancing airway walls and fluid-filled, necrotic bronchial lumen. In the current study, a nodular lung pattern was observed in 5 dogs including one dog with a pulmonary mass. The findings in the dog with the pulmonary mass are similar to the findings described in dogs with EPG[9] with a large with a large mass with honeycomb-like enhancement pattern in the accessory lung lobe and a generalized ground-glass lung pattern.[7]

Histopathologic examination of tissue core biopsies of the lung mass in the present study confirmed a pulmonary eosinophilic granuloma. Although cytologic or histopathologic examination of any of the pulmonary nodules was not performed, they are considered likely to represent eosinophilic granulomas. The differential diagnosis for pulmonary nodules seen on CT in dogs includes secondary and primary lung neoplasia, pulmonary lymphoma, intrathoracic histocytic sarcoma, lymphomatoid granulomatosis, abscess, granulomas of various origin, and haematoceles.[1,7,14] Nodules may be seen with EBP, but additional abnormalities (such as bronchial pathology or concomitant lung pattern) are frequently observed that may help differentiate EBP from neoplastic nodules. Intrathoracic lymphadenopathy was present in nine dogs. This is likely to represent eosinophilic lymphadenitis; however, biopsies were not available for confirmation.

Abnormalities were observed in CT images of all but one dog in the present study, hence finding of a normal CT does not rule out this diagnosis. The dog with a normal-appearing CT had a history of chronic coughing, sneezing and bilateral nasal discharge. The BALF and the bronchial brush analysis found moderate to marked eosinophilic inflammation and epithelial hyperplasia, which were similar in degree to the other dogs in this series.

Occult *Dirifilaria immitis* infection was been reported previously in dogs with EBP[11,12] and EPG[15-17]. Despite the fact of heartworm infection was not ruled out in the patients included in this study, is considered unlikely that heartworm infection could have been in our patients as *Dirofilaria immitis* is rare in the UK and no dogs in this series had a known history of travel to endemic areas. The small pulmonary bulla present in one dog is consistent with a congenital pulmonary bulla and was considered an incidental finding without clinical significance. One dog had mild pleural thickening, this finding is unlikely to be related with the EBP and its clinical significance is unknown.

The histopathological findings and the clinical course observed of dogs with EBP are similar to idiopathic chronic eosinophilic pneumonia (ICEP) and eosinophilic bronchitis (EB) observed in humans.[1] ICEP is a rare disorder of unknown aetiology characterized by chronic cough, respiratory distress, asthenia, alveolar eosinophilia, and characteristic peripheral alveolar infiltrates on imaging.[5,14] EB is a condition characterized in humans by cough responsive to steroids, bronchial eosinophilia, no airway obstruction and normal airway responsiveness.[5,19] The most common CT findings in humans with chronic eosinophilic pneumonia are peripheral airspace consolidation and areas of ground-glass attenuation involving predominantly the peripheral regions of the middle or upper lung zones.[20-22] Clinically and pathologically, canine EBP shares features with human EB and ICEP, with some lesions predominantly involving the bronchi and others primarily involving the pulmonary parenchyma.[5] Similarly, a wide variety of other findings including pulmonary nodules, bronchial wall thickening, bronchiectasis, pleural effusion or thoracic lymphadenopathy may also present in humans with chronic eosinophilic pneumonia.[22]

The main limitation of the present study is relatively low number of cases. The selection of CT for investigation of the present cases was made by the clinician responsible for the case and was based

on numerous factors (including chronicity of the clinical signs), this could potentially lead to selection bias.

We conclude that the CT features of canine EBP are variable and heterogeneous. CT images are abnormal in the majority of affected dogs, hence CT is a useful modality to characterise the nature and distribution of thoracic lesions in dogs with EBP.

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Figure legends

Fig. 1. Computed tomographic findings in dogs with eosinophilic bronchopneumopathy.

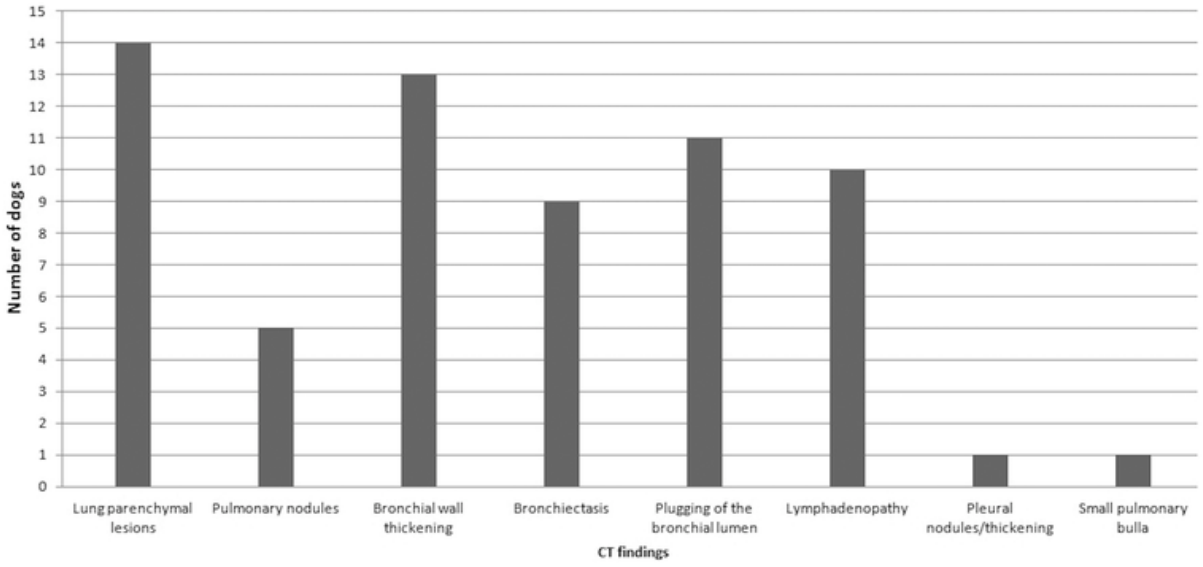

Fig. 2. Non-contrast transverse CT image of a dog with EBP. A rounded soft tissue attenuating nodule is present in right cranial lung lobe (arrow). Note also the multifocal ground glass pattern and bronchial wall thickening.

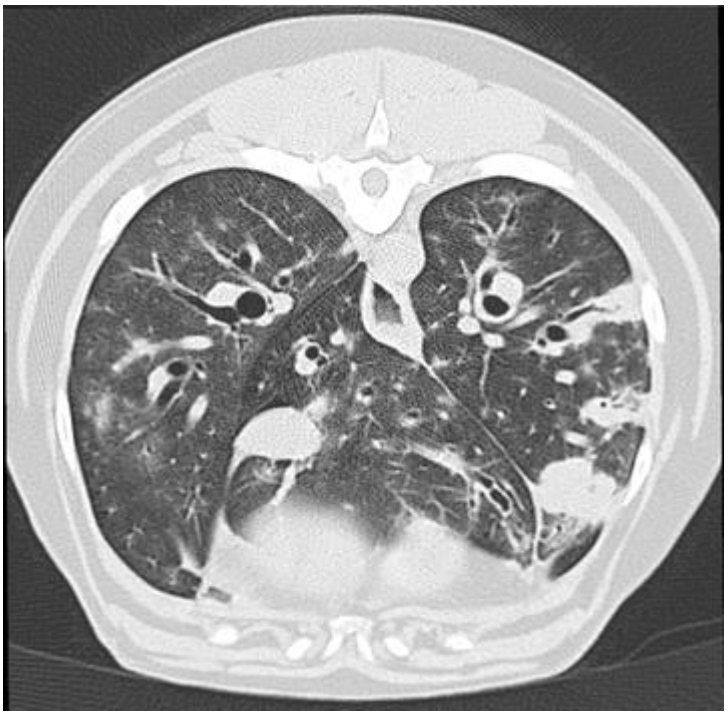

Fig 3. Noncontrast transverse CT image in the lung window of a dog with eosinophilic bronchopneumopathy in the lung window. A rounded soft tissue attenuating nodule is present in right cranial lung lobe (arrow). Note also the multifocal ground glass pattern and bronchial wall thickening.

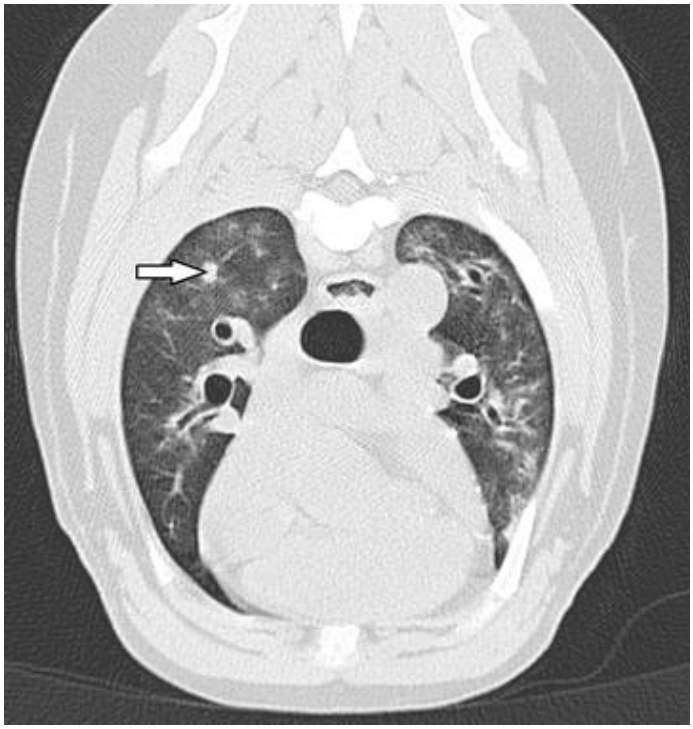

Fig. 4. Pre and postcontrast transverse CT images in the soft tissue window of the dog with a mass with honeycomb-like enhancing in the accessory lung lobe.

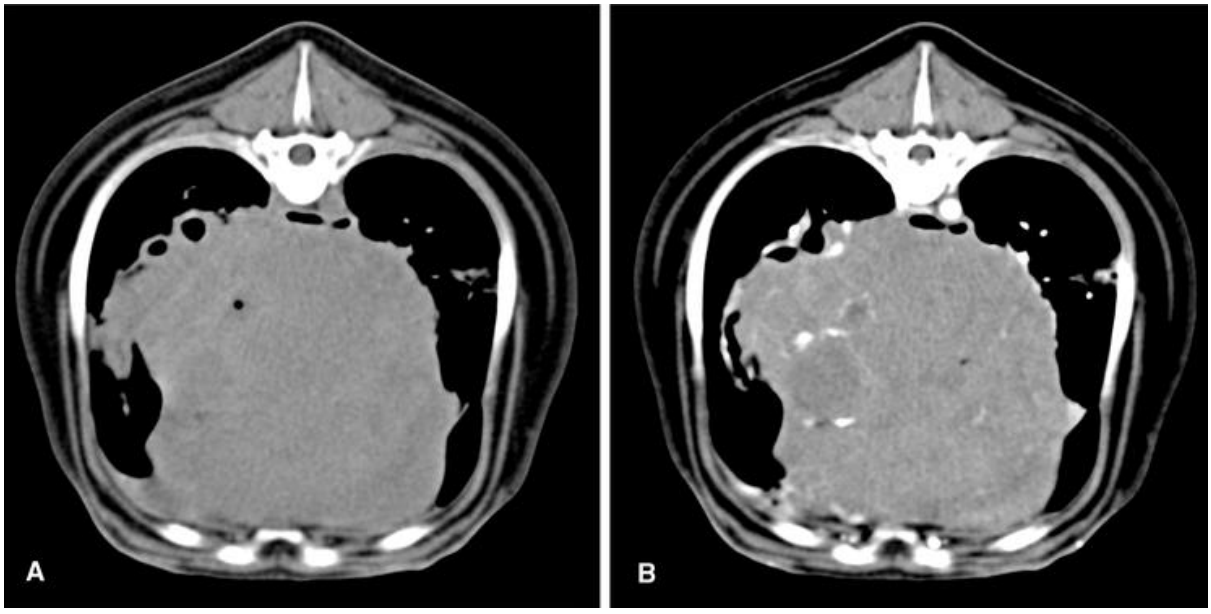

Fig.5. Noncontrast transverse CT image, lung window, of a dog with marked generalized bronchial wall thickening. A generalized ground glass pattern and a focal area of consolidation in the right caudal lung lobe (arrow) are also present.

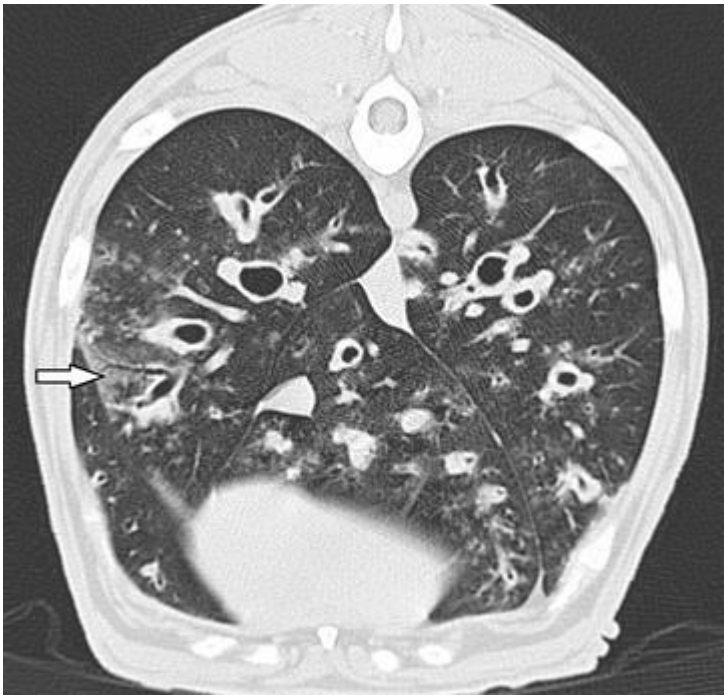

Fig. 6. Noncontrast CT images (sagittal plane multiplanar reconstruction (A) and transverse (B)) in the lung window of a dog with eosinophilic bronchopneumopathy. Note the plugging of the bronchial lumen by mucus/debris of the right caudal (A) and right cranial main bronchus (B).

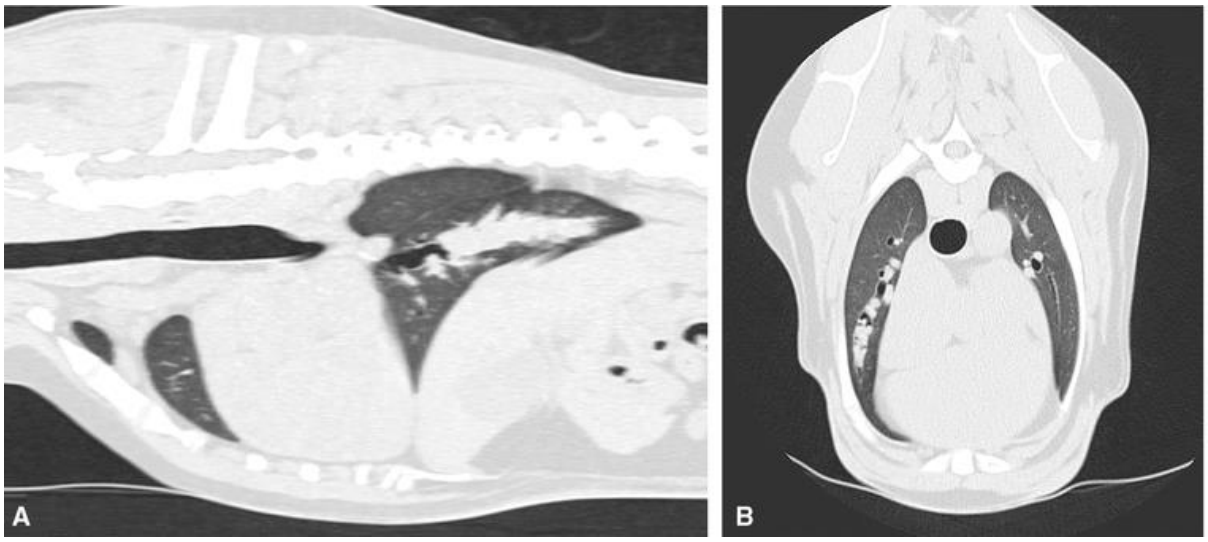

Fig. 7. Minimum intensity projection CT image, lung window, of a dog with cylindrical bronchiectasis affecting the right caudal and the accessory lung lobes. The focal gas attenuation at the tip of the left caudal lung lobe represents an artefact of the intensity projection including gas within the gastric fundus.