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Computed Tomographic Findings in Cats with Mycobacterial Infection

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Abstract

Objectives

The objective of this study was to describe the imaging findings in computed tomography (CT) associated with confirmed mycobacterial infection in cats.

Methods

CT images from 20 cats with confirmed mycobacterial disease were retrospectively reviewed. Five cats underwent conscious full-body CT in a VetMouseTrap™ device. All other cats had thoracic CT performed under general anaesthesia, with the addition of CT investigation of the head/neck, abdomen and limbs in some cases.

Results

Mycobacterial infection was seen most frequently in adult (mean age 7.4 years; range 0.6-14 years) neutered male cats (11/20). The most common infections were *Mycobacterium microti* (6/20) and *Mycobacterium bovis* (6/20). CT abnormalities were most commonly seen in the thorax, consisting of bronchial (9/20), alveolar (8/20), ground glass (6/20) or structured interstitial (15/20) lung patterns, which were often mixed. Tracheobronchial, sternal and cranial mediastinal lymphadenomegaly were common (16/20). Other abnormalities included abdominal (8/13) or peripheral (10/18) lymphadenomegaly, hepatosplenomegaly (7/13), mixed osteolytic/osteoproliferative skeletal lesions (7/20), and cutaneous or subcutaneous soft tissue masses/nodules (4/20).

Conclusions and relevance

CT of feline mycobacteriosis shows a wide range of abnormalities often involving multiple organ systems and mimicking many other feline diseases. Mycobacteriosis

should be considered in the differential diagnosis of thoracic, abdominal and skeletal disorders in cats.

Introduction

Feline mycobacteriosis is a worldwide veterinary health concern, and although definitive data on case numbers worldwide are lacking, mycobacterial infections in cats have been recognised with increasing frequency in the UK, as well as being seen in many other countries. Mycobacterial disease in domestic cats can result from infection by one of a number of species. The most commonly identified mycobacteria include *Mycobacterium microti* and *Mycobacterium bovis*, which are primary pathogens and members of the tuberculous complex group of mycobacteria.[1-3] Non-tuberculous mycobacterial species are less commonly identified within clinically affected cats.[4]

Clinical presentation of mycobacterial infection in cats is variable, and is dependant primarily on the species of mycobacteria involved and, importantly, the route of infection.[2,5-7] Historically, alimentary lesions resulting from ingestion of milk from cows infected with *M. bovis* were most common; however with overall reduction of tuberculosis in the national bovine herd since the early 1900's and widespread pasteurisation of milk this is no longer the case.[8] Single or multiple cutaneous lesions with or without lymph node involvement, and characteristically affecting the so-called 'fight and bite sites' (such as the head and limbs), now represent the most common presentation of mycobacterial infection in cats: they typically result from infection acquired from prey species.[3,9] Infection acquired through inhalation or ingestion, resulting in respiratory or alimentary disease, is seen less frequently. The clinical presentation of these forms of disease, and of disseminated disease resulting from haematogenous spread of infection, can include non-specific signs such as weight loss, anorexia, coughing, anaemia, vomiting/diarrhoea, hepatosplenomegaly, generalised lymphadenopathy and pyrexia.[7]

Definitive diagnosis of mycobacterial disease in cats can present significant problems, in part due to difficulties in sample handling, and limitations in the available laboratory diagnostic techniques. As such, mycobacterial infections are likely underdiagnosed within the domestic cat population. In addition to significant morbidity resulting from primary infection, subclinical infection and recurrence of infection following treatment are common.[7] Since significant and potentially fatal multisystemic disease can result from infection with mycobacterial species, and since there are potential zoonotic risks associated with all members of the tuberculosis complex,[7,10] identification and correct handling of potential cases is of the upmost importance.

Previous publications detailing the diagnostic imaging findings in cats with confirmed mycobacterial infection are limited to a single retrospective case series looking at survey radiographic changes involving 33 cats,[11] and a number of isolated case reports describing the radiographic features of feline mycobacteriosis.[12-14] Computed tomography is increasingly available to the veterinary community, and it offers significant advantages over survey radiography by eliminating superimposition of anatomy, having superior contrast resolution and being able to clarify intrathoracic lesions where radiographic findings are negative or non-specific.[15,16] In addition, the decreased scan times which are achievable with modern multi-detector scanners make CT a valuable tool in investigation of multisystemic disease in clinically compromised patients. The CT features of mycobacterial disease in cats have not been described previously. The aim of this paper was to review CT images from a large number of cats with confirmed mycobacteriosis and to describe the range of abnormalities that can occur.

Materials and Methods

This study comprises a descriptive, retrospective case series. CT studies carried out between August 2009 and January 2015, of cats with confirmed mycobacterial infection were submitted to one of the authors (DGM). Inclusion criteria consisted of: (i) confirmation of mycobacterial infection and (ii) a CT study of diagnostic quality. To confirm mycobacterial involvement, aspirated and/or biopsy samples of affected tissue had been stained with Ziehl-Neelson (ZN) and found to have changes indicative of mycobacteriosis.[1] Where possible, tissue culture,[17] interferon-gamma release assay, or PCR testing had been used to identify which mycobacterial species was involved.[4,18,19]

Pseudonymised CT studies of the confirmed mycobacterial cases were examined without knowledge of specific clinical information by a third year diagnostic imaging resident who was however informed about the topic of the study (AM). To prevent bias by the assumption of disease, CT studies covering the thorax and other body parts from an additional ten cats with confirmed non-mycobacterial diseases were included and also pseudonymised. Images were evaluated using dedicated DICOM viewer software (Osirix, Geneva, Switzerland, version 5.8.5-64bit) on a computer workstation (Apple Mac Pro, Apple, USA) with a calibrated LCD flat screen monitor (Apple Cinemax Display, 30 inch, Apple, USA).

During the course of image evaluation, multi-planar reconstructions, maximum and minimum intensity projections and variable windowing settings were used according to the preferences of the viewer.

CT studies were reviewed for the following diagnostic criteria: bronchial thickening; alveolar pattern; ground glass opacity or structured interstitial lung change; evidence of pleural or pericardial effusion, or pleural/mediastinal thickening; thoracic, abdominal or peripheral lymphadenomegaly, or lymph node mineralisation; abdominal organomegaly, peritoneal effusion, other abdominal organ-associated lesions; osteolysis or osteoproliferative changes; cutaneous/subcutaneous/oral/nasal lesions; vascular and dystrophic soft tissue calcification. The extent of any abnormality was characterised as focal, multifocal, or diffuse. The degree of each change was graded as absent/normal, mild, moderate or severe.

Results

Twenty cats met the inclusion criteria. After all image interpretive data had been collected the additional ten non-mycobacterial cat studies were identified and their data were excluded from further analysis. The most common infections were *M. microti* and *M. bovis*, confirmed in 6/20 cases each. A non-specified *M. tuberculosis* complex species was described in one case and in the remaining 7/20 cases the species involved was not known. Eleven of the 20 cats were neutered males and 9/20 were neutered females. The study group comprised 7/20 Domestic Short Hair, 4/20 Siamese, 2/20 Domestic Long Hair and 1/20 of each of the following; Persian, Birman, Norwegian Forest Cat, Burmilla, British Short Hair, Bengal and Maine Coon cats. The age of one cat was not known. For the remaining cats the mean age was 7.4 ± 3.8 years (range 0.6-14 years).

Five of the 20 cats underwent conscious full-body CT in a specific containing device (VetMouseTrap™, University of Illinois at Urbana-Champaign, Urbana, IL).[20] The remaining 15 cats were scanned under general anaesthesia, with images of the following body regions obtained: thorax only (2), head/neck and thorax (3), thorax and abdomen (4), head/neck, thorax and abdomen (2), head/neck, thorax, abdomen and single forelimb (2), head, thorax, bilateral tarsi/elbows (1), thorax and single hind limb (1).

Intravenous contrast medium (iopamidol or iohexol, 600-700mg I/kg) was administered to 12/20 cats, and post-contrast images of some or all body parts were obtained. Use of contrast medium depended

on the findings in the pre-contrast images, the clinical condition of the cat, and the preferences of the attending radiologist and primary clinician in each case.

Within the evaluated imaging studies, thoracic abnormalities were noted in 19/20 cases. Diffuse bronchial thickening was present in 9/20 cats; being mild in eight cases and moderate in one. Eight cats showed a focal alveolar pattern; mild in two cases, moderate in three cases and severe in three cases (Figure 1(a)). Diffuse or patchy ground glass opacity was noted in 6/20 cats; mild in three cases, moderate in two cases and severe in one case. The most common pulmonary parenchymal change was a diffuse structured interstitial pattern, which was present in 15/20 cats, being either nodular (7/15) or reticulonodular (8/15) in nature; mild in six cases, moderate in five cases and severe in four cases (Figure 1(b,c)). Thoracic CT images of 14/20 cats were considered to show a mixed pulmonary pattern, with a single pattern present in 4/20 cases. The appearance of the pulmonary parenchyma was normal in 2/20 cats, though one of these had a thoracic lymphadenopathy despite normal lungs. Of the 20 cats, 16 had sternal, cranial mediastinal and/or tracheobronchial lymphadenomegaly (Figure 2). Moderate lymphadenomegaly affecting the sternal or tracheobronchial nodes was most common. One cat had moderate mineralisation of an enlarged cranial mediastinal lymph node.

None of the cats had any evidence of pleural or pericardial effusion. One cat showed mild, diffuse pleural thickening. One cat showed mild mineralisation of the aortic root. Two cats had regions of cavitation within the lungs, associated in both cases with focal or multifocal nodular or alveolar changes (Figure 3(a)). Three cats had scattered foci of mineralisation within the lungs, again associated with other focal parenchymal changes (Figure 3(b)).

Thirteen of the 20 cats had imaging studies that included the abdomen. Abdominal lymphadenomegaly was present in 8/13 cases and was typically generalised. The lymph nodes affected could not always be individually identified, but included those of the celiac and cranial mesenteric centres, which variably comprised the hepatic, splenic, gastric, pancreaticoduodenal, jejunal and colic nodes. Lymphadenomegaly was mild in two cats, moderate in four cats and severe in two cats. In one cat with a generalised moderate abdominal lymphadenomegaly, mild mineralisation of a mesenteric lymph node was present (Figure 4(a)). Mild hepatomegaly was present in 3/13 cats and moderate hepatomegaly in 1/13. Mild splenomegaly was present in 6/13 cats and moderate splenomegaly in 1/13. Two cats with

splenomegaly (one mild and one moderate) were also noted to show heterogeneity within the splenic parenchyma following contrast medium administration. Additional abdominal organ changes were noted in 3/13 cats; one had a moderately enlarged pancreas, one had multiple nodules within both kidneys, and one an irregular outline to the left kidney. Peritoneal effusion was not noted in any cat.

The appearance of the peripheral lymph nodes was assessed in 18/20 cats. The two cats not included in this assessment had CT studies of the thorax only, without inclusion of any extra-thoracic lymph node group. In 10/18 cases peripheral lymphadenomegaly was present, mild in 3/18, moderate in 2/18 and severe in 5/18. In 8/10 cats with lymphadenomegaly, the most significant enlargement was noted in the mandibular and medial retropharyngeal nodes (Figure 4(b)); however, multifocal lymphadenomegaly, involving the superficial cervical (prescapular), axillary, inguinal and/or popliteal nodes was variably present. In the other 2/10 cats, the head and neck were not imaged, but enlargement of the superficial cervical and popliteal lymph nodes was noted respectively. Five of the eight cats in which peripheral lymphadenomegaly was not noted underwent conscious CT in the VetMouseTrap™ device and three underwent CT studies which did not include the head and neck.

Focal osteolytic lesions were present in 7/20 cats (although it was not possible to assess the entire skeleton in 15 cats as they did not have full body CT examinations); changes were mild in four cases and moderate in three cases. These lesions affected the nasal bridge in three cats and the limbs in the remaining four, and were predominantly characterised by regions of cortical lysis (5/7) or erosive lesions at joint surfaces (2/7) (Figure 5). An associated pathological long bone fracture was present in one case. In all but one of these cases osteoproliferative changes, either periosteal reaction or periarticular osteophytosis, were noted in the same location as the osteolytic change. The osteoproliferation was mild in three cases and severe in three cases; however, the degree of proliferative change did not necessarily correlate with the degree of lytic change in each case.

Cutaneous or subcutaneous lesions were only infrequently present within the studies evaluated. Focal mass lesions over the nasal bridge were noted in 2/20 cats, graded moderate in one and severe in one. One other cat had a small amount of fluid accumulation and soft tissue thickening in the dorsal nasal chambers. Each of these lesions was adjacent to bony abnormalities. A focal, but extensive, mass lesion was noted along the ventral head and neck of one cat. One cat was found to have multiple, widely

distributed, subcutaneous nodules. Diffuse extra-thoracic dystrophic soft tissue mineralisation was not noted in any cat.

Discussion

Mycobacteriosis in cats is known to be a highly variable disease, and should always be considered as a possible differential diagnosis in cases which present with multisystemic signs. Mycobacterial disease is likely under-recognised, primarily due to a lack of awareness of the full spectrum of changes which can be associated with it.

Mycobacterial infection is most commonly seen in adult, neutered male cats consistent with the results of our study.[9] Domestic Short Hair cats predominate in our study, but to a lesser degree than noted in the previous radiographic case series (36% vs 87%).[11] The reason for this is unknown, but may reflect a higher proportion of pedigree cats within a referral population, which are therefore more likely to undergo advanced imaging.

CT abnormalities of the thorax were commonly noted, being present in all but one cat. However, multisystemic abnormalities were also common, with changes affecting more than one anatomical region in all but five cases. Of these five, three had abnormalities detected on clinical examination which were not appreciable on the CT images. In cats, systemic mycobacterial infection is most commonly caused by *M. bovis* or *M microti*,[3,9,21-24] and our results are consistent with this.

Previous reports of radiographic findings in cats with mycobacterial disease described a mild predominance of a mixed lung pattern (ie, a combination of bronchial, alveolar and/or interstitial changes),[1,9,11-13,22-24] but distinct alveolar, bronchial or interstitial patterns in isolation were also identified.[11] Interestingly, where cases in our study displayed mixed lung patterns, bronchial thickening and ground glass opacity were most commonly graded as mild, whereas alveolar pattern and structured interstitial patterns were more likely to be moderate or severe. This is interesting for two reasons. Firstly, the mild bronchial and unstructured interstitial patterns are of a degree that comparable changes may not be easily visible radiographically, or may be attributed to expiratory or underexposed radiographs, or superimposition of other structures. In a radiographic study it is therefore possible that only a more significant overlying alveolar or nodular pattern may be recognised, leading to classification as a single

lung pattern. As superimposition effects are eliminated by CT, it becomes easier to identify these mild changes in addition to the more marked ones. Secondly, a mild bronchial or unstructured interstitial pattern may be indicative of concurrent conditions, such as low-grade allergic airway disease, rather than being directly related to an active mycobacterial infection.[25,26] Differentiation of these may not be possible.

Within our study, the most commonly encountered single lung pattern was structured interstitial. However, these cases could be further subdivided into cases displaying a nodular pattern, comprising scattered rounded hyperattenuating foci, and a reticulonodular pattern, where rounded foci and linear or sickle-shaped hyperattenuating structures overlie to give a more complex overall pattern. In humans, a faint, diffuse reticulonodular pattern is considered characteristic of miliary tuberculosis.[27] While nodular and reticulonodular patterns are distinguishable on good quality radiographs in cats, the distinction is only rarely made in veterinary imaging. On CT however, the difference is more easily appreciable. The diagnostic and prognostic significance of the variable patterns in feline patients is currently unknown, but certainly warrants further investigation, as a structured interstitial pattern is a common finding in many feline lung pathologies (eg, pulmonary fibrosis, metastatic neoplasia, eosinophilic bronchopneumopathy and a wide range of infectious pneumonias).

It is interesting to note that within our study population, two cats were found to have cavitations within their lungs. While this feature is relatively common in both humans and dogs with tuberculosis[28-30] it was not noted in any case in the previous radiographic study of cats,[11] and the only paper which describes cavitating tubercles in cats was published in 1949.[5] The lesions noted in the two cats in this study were small (<1 cm) and were contained within regions of nodular or alveolar change. It is possible therefore that they may not have been visible on radiographs, again highlighting the advantage of cross sectional imaging. Alternatively, this may indeed reflect a rare occurrence in feline patients, which has occurred coincidentally within our study population. In either case, it is an important characteristic to recognise, as cavitated lung masses are occasionally identified in feline patients with lung neoplasia,[16,25] and the potential for misdiagnosis exists in cats with mycobacteriosis which show this feature. In addition this should be recognised because these cats likely pose an increased zoonotic risk compared with those showing the more typical structured interstitial pattern as they may allow mycobacteria to gain access to the upper airways.

Thoracic lymphadenomegaly is a feature of numerous pulmonary and multisystemic conditions in cats including, but not limited to, infiltrative and metastatic neoplasia, hypereosinophilic syndromes and systemic mycosis/bacteriosis.[31] As expected thoracic lymphadenomegaly was commonly noted within our study population, but in contrast to the findings of the previous radiographic paper, mild and moderate enlargement predominated over severe.[11] This may reflect the difficulty in recognising minor changes on radiographs. It is also worth noting that even given the superior contrast resolution of CT, with mild lymphadenomegaly, particularly in the perihilar region; changes were more easily appreciated in post-contrast studies when compared with pre-contrast. This suggests that there is value in performing post-contrast scans in all cases (unless there is a clinical contraindication), which was not standard practice within our study population.

Mineralisation of thoracic lymph nodes and pulmonary parenchyma can result from chronic inflammation associated with mycobacterial infection;[9,13,32] it is also seen in cases of both primary and metastatic pulmonary neoplasia, and chronic airways disease.[25] In either case, it is a finding which most likely relates to the disease process that is present. In contrast, mild aortic root calcification, such as that seen in one case (a seven year old cat) in our study is, in our experience, an occasional finding in middle aged to older cats, and not necessarily related to clinical disease.

While peripheral and abdominal lymphadenomegaly were relatively common within the study population, it is possible that the number of cases with mild or moderate lymphadenomegaly in the head and neck was artificially low. This is because all cases recorded as having normal peripheral lymph nodes on physical examination either did not undergo imaging of the head and neck, or were scanned conscious within a VetMouseTrap™ device. The protocol for these scans involved a short scan time (in order to minimise movement) resulting in a relatively large slice thickness and consequently a reduced longitudinal resolution. This can compromise assessment of small structures so it is possible that mild or moderate abnormalities of the head and neck, such as lymphadenomegaly, may have been overlooked. Other abdominal changes such as hepatomegaly, splenomegaly, renal and pancreatic changes were noted relatively infrequently and were mild or moderate in extent, consistent with previous reports.[9,11,12,33]

Two distinct manifestations of skeletal disease were noted within our population. The lesions characterised by cortical lysis likely represent sites of primary bacterial inoculation and as such are

consistent in location with ’fight and bite’ injuries; whereas periarticular abnormalities are consistent with an infectious polyarthritis resulting from haematogenous dissemination of bacteria. It is interesting to note that the appendicular skeletal lesions in this study were clinically evident, and affected regions were intentionally included in the imaging studies. Clinically silent skeletal lesions may have been overlooked as the limbs were excluded from the majority of studies. The only studies in which the limbs were included in full were those performed using the VetMouseTrap™ device and it is possible that subtle or focal regions of bone lysis or proliferation may not have been recognised due to the lower resolution of these studies.

Cutaneous lesions were noted infrequently in this study. While this may initially seem surprising, given that cutaneous lesions represent a common presentation of mycobacteriosis,[3,9] it reflects the fact that CT imaging is more likely to be employed in cases presenting with systemic disease, or used as a staging tool in cats with clinically evident focal skin lesions without requirement for imaging of the lesions themselves. The presence of intranasal changes in one cat is interesting, as these are indicative of a mycobacterial rhinitis, a manifestation of respiratory mycobacteriosis which may not be commonly recognised.

There are a number of limitations to this study. The most significant of these is that although mycobacteriosis was confirmed in each case, histopathology on all involved tissues was not typically performed; therefore, it is not possible to confirm that all changes seen were due to mycobacterial infection. Due to the inherent difficulties in confirmation of mycobacterial infection, the time lapse between acquisition of CT images and definitive confirmation of diagnosis was very variable; it extended to four years and nine months in one case (though a lapse of one to four months was more typical). In all cases however, at the time of imaging, the combination of clinical and pathological findings gave sufficient confidence in the diagnosis to allow treatment to be instigated; imaging was used to stage the cases and so guide the intensity and duration of treatment. The evolution of changes over time in association with treatment has not been described, and will be interesting to explore in the future. Finally, given the retrospective nature of this study there are inconsistencies between cases with respect to factors such as regions imaged and use of contrast medium. This leads to a bias in our results, and may underestimate subclinical disease, particularly affecting the peripheral structures. As mentioned, the limited resolution of smaller structures on VetMouseTrap™ scans contributes to this. However, the advantages of this technique

for disease screening, particularly in clinically compromised patients should not be ignored, and as faster scanners become more commonplace many of the resolution difficulties will be eliminated.

Conclusions

As expected, the majority of CT changes noted in this study represent multisystemic disease, typically with combinations of pulmonary infiltration, lymphadenomegaly and organomegaly. These changes are strongly suggestive of infiltrative disease, differentials for which can include neoplasia (such as lymphoma or mast cell disease), chronic inflammation/infectious processes (mycobacteriosis, feline infectious peritonitis or systemic mycosis), hypereosinophilic syndrome and amyloidosis.[24] While no abnormality has been recognised that is specific for mycobacteriosis, it is important that the potential for mycobacterial infection is considered when these types of changes are identified in feline patients, especially if they have non-specific clinical signs. In addition, when managing patients with a diagnosis of mycobacteriosis, the potential for widespread clinical and sub-clinical abnormalities must be considered and investigated in full.

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Computed Tomographic Findings in Cats with Mycobacterial Infection

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Abstract

Objectives

The objective of this study was to describe the imaging findings in computed tomography (CT) associated with confirmed mycobacterial infection in cats.

Methods

CT images from 20 cats with confirmed mycobacterial disease were retrospectively reviewed. Five cats underwent conscious full-body CT in a VetMouseTrap™ device. All other cats had thoracic CT performed under general anaesthesia, with the addition of CT investigation of the head/neck, abdomen and limbs in some cases.

Results

Mycobacterial infection was seen most frequently in adult (mean age 7.4 years; range 0.6-14 years) neutered male cats (11/20). The most common infections were *Mycobacterium microti* (6/20) and *Mycobacterium bovis* (6/20). CT abnormalities were most commonly seen in the thorax, consisting of bronchial (9/20), alveolar (8/20), ground glass (6/20) or structured interstitial (15/20) lung patterns, which were often mixed. Tracheobronchial, sternal and cranial mediastinal lymphadenomegaly were common (16/20). Other abnormalities included abdominal (8/13) or peripheral (10/18) lymphadenomegaly, hepatosplenomegaly (7/13), mixed osteolytic/osteoproliferative skeletal lesions (7/20), and cutaneous or subcutaneous soft tissue masses/nodules (4/20).

Conclusions and relevance

CT of feline mycobacteriosis shows a wide range of abnormalities often involving multiple organ systems and mimicking many other feline diseases. Mycobacteriosis

should be considered in the differential diagnosis of thoracic, abdominal and skeletal disorders in cats.

Introduction

Feline mycobacteriosis is a worldwide veterinary health concern, and although definitive data on case numbers worldwide are lacking, mycobacterial infections in cats have been recognised with increasing frequency in the UK, as well as being seen in many other countries. Mycobacterial disease in domestic cats can result from infection by one of a number of species. The most commonly identified mycobacteria include *Mycobacterium microti* and *Mycobacterium bovis*, which are primary pathogens and members of the tuberculous complex group of mycobacteria.[1-3] Non-tuberculous mycobacterial species are less commonly identified within clinically affected cats.[4]

Clinical presentation of mycobacterial infection in cats is variable, and is dependant primarily on the species of mycobacteria involved and, importantly, the route of infection.[2,5-7] Historically, alimentary lesions resulting from ingestion of milk from cows infected with *M. bovis* were most common; however with overall reduction of tuberculosis in the national bovine herd since the early 1900's and widespread pasteurisation of milk this is no longer the case.[8] Single or multiple cutaneous lesions with or without lymph node involvement, and characteristically affecting the so-called 'fight and bite sites' (such as the head and limbs), now represent the most common presentation of mycobacterial infection in cats: they typically result from infection acquired from prey species.[3,9] Infection acquired through inhalation or ingestion, resulting in respiratory or alimentary disease, is seen less frequently. The clinical presentation of these forms of disease, and of disseminated disease resulting from haematogenous spread of infection, can include non-specific signs such as weight loss, anorexia, coughing, anaemia, vomiting/diarrhoea, hepatosplenomegaly, generalised lymphadenopathy and pyrexia.[7]

Definitive diagnosis of mycobacterial disease in cats can present significant problems, in part due to difficulties in sample handling, and limitations in the available laboratory diagnostic techniques. As such, mycobacterial infections are likely underdiagnosed within the domestic cat population. In addition to significant morbidity resulting from primary infection, subclinical infection and recurrence of infection following treatment are common.[7] Since significant and potentially fatal multisystemic disease can result from infection with mycobacterial species, and since there are potential zoonotic risks associated with all members of the tuberculosis complex,[7,10] identification and correct handling of potential cases is of the upmost importance.

Previous publications detailing the diagnostic imaging findings in cats with confirmed mycobacterial infection are limited to a single retrospective case series looking at survey radiographic changes involving 33 cats,[11] and a number of isolated case reports describing the radiographic features of feline mycobacteriosis.[12-14] Computed tomography is increasingly available to the veterinary community, and it offers significant advantages over survey radiography by eliminating superimposition of anatomy, having superior contrast resolution and being able to clarify intrathoracic lesions where radiographic findings are negative or non-specific.[15,16] In addition, the decreased scan times which are achievable with modern multi-detector scanners make CT a valuable tool in investigation of multisystemic disease in clinically compromised patients. The CT features of mycobacterial disease in cats have not been described previously. The aim of this paper was to review CT images from a large number of cats with confirmed mycobacteriosis and to describe the range of abnormalities that can occur.

Materials and Methods

This study comprises a descriptive, retrospective case series. CT studies carried out between August 2009 and January 2015, of cats with confirmed mycobacterial infection were submitted to one of the authors (DGM). Inclusion criteria consisted of: (i) confirmation of mycobacterial infection and (ii) a CT study of diagnostic quality. To confirm mycobacterial involvement, aspirated and/or biopsy samples of affected tissue had been stained with Ziehl-Neelson (ZN) and found to have changes indicative of mycobacteriosis.[1] Where possible, tissue culture,[17] interferon-gamma release assay, or PCR testing had been used to identify which mycobacterial species was involved.[4,18,19]

Pseudonymised CT studies of the confirmed mycobacterial cases were examined without knowledge of specific clinical information by a third year diagnostic imaging resident who was however informed about the topic of the study (AM). To prevent bias by the assumption of disease, CT studies covering the thorax and other body parts from an additional ten cats with confirmed non-mycobacterial diseases were included and also pseudonymised. Images were evaluated using dedicated DICOM viewer software (Osirix, Geneva, Switzerland, version 5.8.5-64bit) on a computer workstation (Apple Mac Pro, Apple, USA) with a calibrated LCD flat screen monitor (Apple Cinemax Display, 30 inch, Apple, USA).

During the course of image evaluation, multi-planar reconstructions, maximum and minimum intensity projections and variable windowing settings were used according to the preferences of the viewer.

CT studies were reviewed for the following diagnostic criteria: bronchial thickening; alveolar pattern; ground glass opacity or structured interstitial lung change; evidence of pleural or pericardial effusion, or pleural/mediastinal thickening; thoracic, abdominal or peripheral lymphadenomegaly, or lymph node mineralisation; abdominal organomegaly, peritoneal effusion, other abdominal organ-associated lesions; osteolysis or osteoproliferative changes; cutaneous/subcutaneous/oral/nasal lesions; ~~or~~ vascular and dystrophic soft tissue calcification. The extent of any abnormality was characterised as focal, multifocal, or diffuse. The degree of each change was graded as absent/normal, mild, moderate or severe.

Results

Twenty cats met the inclusion criteria. After all image interpretive data had been collected the additional ten non-mycobacterial cat studies were identified and their data were excluded from further analysis. The most common infections were *M. microti* and *M. bovis*, confirmed in 6/20 cases each. A non-specified *M. tuberculosis* complex species was described in one case and in the remaining 7/20 cases the species involved was not known. Eleven of the 20 cats were neutered males and 9/20 were neutered females. The study group comprised 7/20 Domestic Short Hair, 4/20 Siamese, 2/20 Domestic Long Hair and 1/20 of each of the following; Persian, Birman, Norwegian Forest Cat, Burmilla, British Short Hair, Bengal and Maine Coon cats. The age of one cat was not known. For the remaining cats the mean age was 7.4 ± 3.8 years (range 0.6-14 years).

Five of the 20 cats underwent conscious full-body CT in a specific containing device (VetMouseTrap™, University of Illinois at Urbana-Champaign, Urbana, IL).[20] The remaining 15 cats were scanned under general anaesthesia, with images of the following body regions obtained: thorax only (2), head/neck and thorax (3), thorax and abdomen (4), head/neck, thorax and abdomen (2), head/neck, thorax, abdomen and single forelimb (2), head, thorax, bilateral tarsi/elbows (1), thorax and single hind limb (1).

Intravenous contrast medium (iopamidol or iohexol, 600-700mg I/kg) was administered to 12/20 cats, and post-contrast images of some or all body parts were obtained. Use of contrast medium depended

on the findings in the pre-contrast images, the clinical condition of the cat, and the preferences of the attending radiologist and primary clinician in each case.

Within the evaluated imaging studies, thoracic abnormalities were noted in 19/20 cases. Diffuse bronchial thickening was present in 9/20 cats; being mild in eight cases and moderate in one. Eight cats showed a focal alveolar pattern; mild in two cases, moderate in three cases and severe in three cases (Figure 1(a)). Diffuse or patchy ground glass opacity was noted in 6/20 cats; mild in three cases, moderate in two cases and severe in one case. The most common pulmonary parenchymal change was a diffuse structured interstitial pattern, which was present in 15/20 cats, being either nodular (7/15) or reticulonodular (8/15) in nature; mild in six cases, moderate in five cases and severe in four cases (Figure 1(b,c)). Thoracic CT images of 14/20 cats were considered to show a mixed pulmonary pattern, with a single pattern present in 4/20 cases. The appearance of the pulmonary parenchyma was normal in 2/20 cats, though one of these had a thoracic lymphadenopathy despite normal lungs. Of the 20 cats, 16 had sternal, cranial mediastinal and/or tracheobronchial lymphadenomegaly (Figure 2). Moderate lymphadenomegaly affecting the sternal or tracheobronchial nodes was most common. One cat had moderate mineralisation of an enlarged cranial mediastinal lymph node.

None of the cats had any evidence of pleural or pericardial effusion. One cat showed mild, diffuse pleural thickening. One cat showed mild mineralisation of the aortic root. Two cats had regions of cavitation within the lungs, associated in both cases with focal or multifocal nodular or alveolar changes (Figure 3(a)). Three cats had scattered foci of mineralisation within the lungs, again associated with other focal parenchymal changes (Figure 3(b)).

Thirteen of the 20 cats had imaging studies that included the abdomen. Abdominal lymphadenomegaly was present in 8/13 cases and was typically generalised~~diffuse~~. The lymph nodes affected could not always be individually identified, but included those of the celiac and cranial mesenteric centres, which variably comprised the hepatic, splenic, gastric, pancreaticoduodenal, jejunal and colic nodes. Lymphadenomegaly was mild in two cats, moderate in four cats and severe in two cats. In one cat with a generalised moderate abdominal lymphadenomegaly, mild mineralisation of a mesenteric lymph node was present (Figure 4(a)). Mild hepatomegaly was present in 3/13 cats and moderate hepatomegaly in 1/13. Mild splenomegaly was present in 6/13 cats and moderate splenomegaly in 1/13. Two cats with

splenomegaly (one mild and one moderate) were also noted to show heterogeneity within the splenic parenchyma following contrast medium administration. Additional abdominal organ changes were noted in 3/13 cats; one had a moderately enlarged pancreas, one had multiple nodules within both kidneys, and one an irregular outline to the left kidney. Peritoneal effusion was not noted in any cat.

The appearance of the peripheral lymph nodes was assessed in 18/20 cats. The two cats not included in this assessment had CT studies of the thorax only, without inclusion of any extra-thoracic lymph node group. In 10/18 cases peripheral lymphadenomegaly was present, mild in 3/18, moderate in 2/18 and severe in 5/18. In 8/10 cats with lymphadenomegaly, the most significant enlargement was noted in the mandibular and medial retropharyngeal nodes (Figure 4(b)); however, multifocal ~~more diffuse~~ lymphadenomegaly, involving the superficial cervical (prescapular), axillary, inguinal and/or popliteal nodes was variably present. In the other 2/10 cats, the head and neck were not imaged, but enlargement of the superficial cervical and popliteal lymph nodes was noted respectively. Five of the eight cats in which peripheral lymphadenomegaly was not noted underwent conscious CT in the VetMouseTrap™ device and three underwent CT studies which did not include the head and neck.

Focal osteolytic lesions were present in 7/20 cats (although it was not possible to assess the entire skeleton in 15 cats as they did not have full body CT examinations); changes were mild in four cases and moderate in three cases. These lesions affected the nasal bridge in three cats and the limbs in the remaining four, and were predominantly characterised by regions of cortical lysis (5/7) or erosive lesions at joint surfaces (2/7) (Figure 5). An associated pathological long bone fracture was present in one case. In all but one of these cases osteoproliferative changes, either periosteal reaction or periarticular osteophytosis, were noted in the same location as the osteolytic change. The osteoproliferation was mild in three cases and severe in three cases; however, the degree of proliferative change did not necessarily correlate with the degree of lytic change in each case.

Cutaneous or subcutaneous lesions were only infrequently present within the studies evaluated. Focal mass lesions over the nasal bridge were noted in 2/20 cats, graded moderate in one and severe in one. One other cat had a small amount of fluid accumulation and soft tissue thickening in the dorsal nasal chambers. Each of these lesions was adjacent to bony abnormalities. A focal, but extensive, mass lesion was noted along the ventral head and neck of one cat. One cat was found to have multiple, widely

distributed, subcutaneous nodules. Diffuse extra-thoracic dystrophic soft tissue mineralisation was not noted in any cat.

Discussion

Mycobacteriosis in cats is known to be a highly variable disease, and should always be considered as a possible differential diagnosis in cases which present with multisystemic signs. Mycobacterial disease is likely under-recognised, primarily due to a lack of awareness of the full spectrum of changes which can be associated with it.

Mycobacterial infection is most commonly seen in adult, neutered male cats consistent with the results of our study.[9] Domestic Short Hair cats predominate in our study, but to a lesser degree than noted in the previous radiographic case series (36% vs 87%).[11] The reason for this is unknown, but may reflect a higher proportion of pedigree cats within a referral population, which are therefore more likely to undergo advanced imaging.

CT abnormalities of the thorax were commonly noted, being present in all but one cat. However, multisystemic abnormalities were also common, with changes affecting more than one anatomical region in all but five cases. Of these five, three had abnormalities detected on clinical examination which were not appreciable on the CT images. In cats, systemic mycobacterial infection is most commonly caused by *M. bovis* or *M microti*,[3,9,21-24] and our results are consistent with this.

Previous reports of radiographic findings in cats with mycobacterial disease described a mild predominance of a mixed lung pattern (ie, a combination of bronchial, alveolar and/or interstitial changes),[1,9,11-13,22-24] but distinct alveolar, bronchial or interstitial patterns in isolation were also identified.[11] Interestingly, where cases in our study displayed mixed lung patterns, bronchial thickening and ground glass opacity were most commonly graded as mild, whereas alveolar pattern and structured interstitial patterns were more likely to be moderate or severe. This is interesting for two reasons. Firstly, the mild bronchial and unstructured interstitial patterns are of a degree that comparable changes may not be easily visible radiographically, or may be attributed to expiratory or underexposed radiographs, or superimposition of other structures. In a radiographic study it is therefore possible that only a more significant overlying alveolar or nodular pattern may be recognised, leading to classification as a single

lung pattern. As superimposition effects are eliminated by CT, it becomes easier to identify these mild changes in addition to the more marked ones. Secondly, a mild bronchial or unstructured interstitial pattern may be indicative of concurrent conditions, such as low-grade allergic airway disease, rather than being directly related to an active mycobacterial infection.[25,26] Differentiation of these may not be possible.

Within our study, the most commonly encountered single lung pattern was structured interstitial. However, these cases could be further subdivided into cases displaying a nodular pattern, comprising scattered rounded hyperattenuating foci, and a reticulonodular pattern, where rounded foci and linear or sickle-shaped hyperattenuating structures overlie to give a more complex overall pattern. In humans, a faint, diffuse reticulonodular pattern is considered characteristic of miliary tuberculosis.[27] While nodular and reticulonodular patterns are distinguishable on good quality radiographs in cats, the distinction is only rarely made in veterinary imaging. On CT however, the difference is more easily appreciable. The diagnostic and prognostic significance of the variable patterns in feline patients is currently unknown, but certainly warrants further investigation, as a structured interstitial pattern is a common finding in many feline lung pathologies (eg, pulmonary fibrosis, metastatic neoplasia, eosinophilic bronchopneumopathy and a wide range of infectious pneumonias).

It is interesting to note that within our study population, two cats were found to have cavitations within their lungs. While this feature is relatively common in both humans and dogs with tuberculosis[28-30] it was not noted in any case in the previous radiographic study of cats,[11] and the only paper which describes cavitating tubercles in cats was published in 1949.[5] The lesions noted in the two cats in this study were small (<1 cm) and were contained within regions of nodular or alveolar change. It is possible therefore that they may not have been visible on radiographs, again highlighting the advantage of cross sectional imaging. Alternatively, this may indeed reflect a rare occurrence in feline patients, which has occurred coincidentally within our study population. In either case, it is an important characteristic to recognise, as cavitated lung masses are occasionally identified in feline patients with lung neoplasia,[16,25] and the potential for misdiagnosis exists in cats with mycobacteriosis which show this feature. In addition this should be recognised because these cats likely pose an increased zoonotic risk compared with those showing the more typical structured interstitial pattern as they may allow mycobacteria to gain access to the upper airways.

Thoracic lymphadenomegaly is a feature of numerous pulmonary and multisystemic conditions in cats including, but not limited to, infiltrative and metastatic neoplasia, hypereosinophilic syndromes and systemic mycosis/bacteriosis.[31] As expected thoracic lymphadenomegaly was commonly noted within our study population, but in contrast to the findings of the previous radiographic paper, mild and moderate enlargement predominated over severe.[11] This may reflect the difficulty in recognising minor changes on radiographs. It is also worth noting that even given the superior contrast resolution of CT, with mild lymphadenomegaly, particularly in the perihilar region; changes were more easily appreciated in post-contrast studies when compared with pre-contrast. This suggests that there is value in performing post-contrast scans in all cases (unless there is a clinical contraindication), which was not standard practice within our study population.

Mineralisation of thoracic lymph nodes and pulmonary parenchyma can result from chronic inflammation associated with mycobacterial infection;[9,13,32] it is also seen in cases of both primary and metastatic pulmonary neoplasia, and chronic airways disease.[25] In either case, it is a finding which most likely relates to the disease process that is present. In contrast, mild aortic root calcification, such as that seen in one case (a seven year old cat) in our study is, in our experience, an occasional finding in middle aged to older cats, and not necessarily related to clinical disease.

While peripheral and abdominal lymphadenomegaly were relatively common within the study population, it is possible that the number of cases with mild or moderate lymphadenomegaly in the head and neck was artificially low. This is because all cases recorded as having normal peripheral lymph nodes on physical examination either did not undergo imaging of the head and neck, or were scanned conscious within a VetMouseTrap™ device. The protocol for these scans involved a short scan time (in order to minimise movement) resulting in a relatively large slice thickness and consequently a reduced longitudinal resolution. This can compromise assessment of small structures so it is possible that mild or moderate abnormalities of the head and neck, such as lymphadenomegaly, may have been overlooked. Other abdominal changes such as hepatomegaly, splenomegaly, renal and pancreatic changes were noted relatively infrequently and were mild or moderate in extent, consistent with previous reports.[9,11,12,33]

Two distinct manifestations of skeletal disease were noted within our population. The lesions characterised by cortical lysis likely represent sites of primary bacterial inoculation and as such are

consistent in location with ’fight and bite’ injuries; whereas periarticular abnormalities are consistent with an infectious polyarthritis resulting from haematogenous dissemination of bacteria. It is interesting to note that the appendicular skeletal lesions in this study were clinically evident, and affected regions were intentionally included in the imaging studies. Clinically silent skeletal lesions may have been overlooked as the limbs were excluded from the majority of studies. The only studies in which the limbs were included in full were those performed using the VetMouseTrap™ device and it is possible that subtle or focal regions of bone lysis or proliferation may not have been recognised due to the lower resolution of these studies.

Cutaneous lesions were noted infrequently in this study. While this may initially seem surprising, given that cutaneous lesions represent a common presentation of mycobacteriosis,[3,9] it reflects the fact that CT imaging is more likely to be employed in cases presenting with systemic disease, or used as a staging tool in cats with clinically evident focal skin lesions without requirement for imaging of the lesions themselves. The presence of intranasal changes in one cat is interesting, as these are indicative of a mycobacterial rhinitis, a manifestation of respiratory mycobacteriosis which may not be commonly recognised.

There are a number of limitations to this study. The most significant of these is that although mycobacteriosis was confirmed in each case, histopathology on all involved tissues was not typically performed; therefore, it is not possible to confirm that all changes seen were due to mycobacterial infection. Due to the inherent difficulties in confirmation of mycobacterial infection, the time lapse between acquisition of CT images and definitive confirmation of diagnosis was very variable; it extended to four years and nine months in one case (though a lapse of one to four months was more typical). In all cases however, at the time of imaging, the combination of clinical and pathological findings gave sufficient confidence in the diagnosis to allow treatment to be instigated; imaging was used to stage the cases and so guide the intensity and duration of treatment. The evolution of changes over time in association with treatment has not been described, and will be interesting to explore in the future. Finally, given the retrospective nature of this study there are inconsistencies between cases with respect to factors such as regions imaged and use of contrast medium. This leads to a bias in our results, and may underestimate subclinical disease, particularly affecting the peripheral structures. As mentioned, the limited resolution of smaller structures on VetMouseTrap™ scans contributes to this. However, the advantages of this technique

for disease screening, particularly in clinically compromised patients should not be ignored, and as faster scanners become more commonplace many of the resolution difficulties will be eliminated.

Conclusions

As expected, the majority of CT changes noted in this study represent multisystemic disease, typically with combinations of pulmonary infiltration, lymphadenomegaly and organomegaly. These changes are strongly suggestive of infiltrative disease, differentials for which can include neoplasia (such as lymphoma or mast cell disease), chronic inflammation/infectious processes (mycobacteriosis, feline infectious peritonitis or systemic mycosis), hypereosinophilic syndrome and amyloidosis.[24] While no abnormality has been recognised that is specific for mycobacteriosis, it is important that the potential for mycobacterial infection is considered when these types of changes are identified in feline patients, especially if they have non-specific clinical signs. In addition, when managing patients with a diagnosis of mycobacteriosis, the potential for widespread clinical and sub-clinical abnormalities must be considered and investigated in full.

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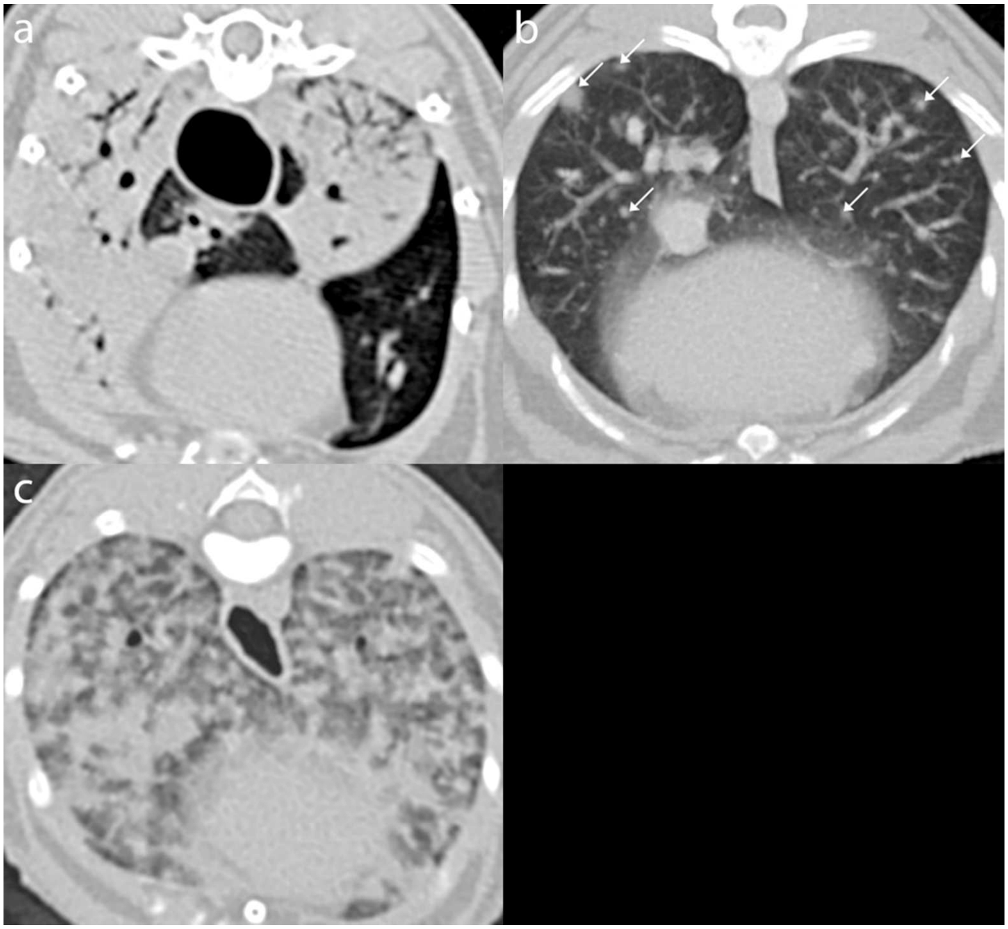

Figure 1. CT appearance of lung parenchyma in three cats with mycobacteriosis, at the level of the accessory lung lobe. (a) Alveolar pattern affecting multiple lung lobes. (b) Diffuse structured interstitial pattern comprising multiple relatively well defined nodules (arrows). (c) Diffuse structured interstitial pattern comprising mixed nodular and linear structures, characteristic of a reticulonodular pattern
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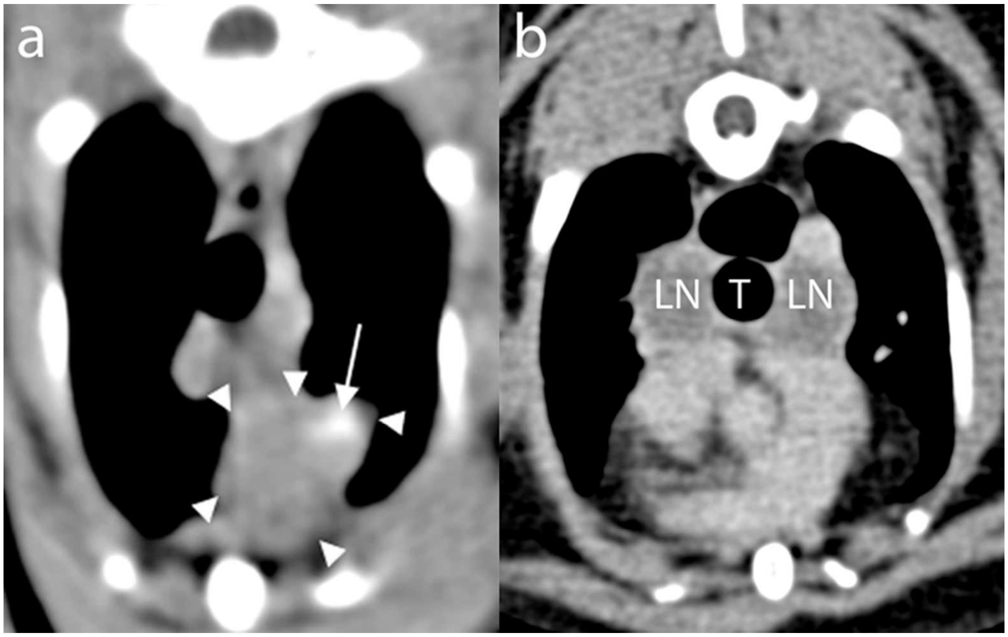

Figure 2. Thoracic lymphadenopathy in two cats with mycobacteriosis. (a) Transverse thoracic CT image at the level of the third sternebra showing an enlarged cranial mediastinal lymph node (arrowheads) containing a focus of mineralisation (arrow). (b) Post-contrast transverse CT image at the level of the cardiac base showing bilaterally enlarged tracheobronchial lymph nodes (LN) surrounding the trachea (T). The use of contrast medium allows differentiation from the cardiac and vascular structures
134x84mm (300 x 300 DPI)

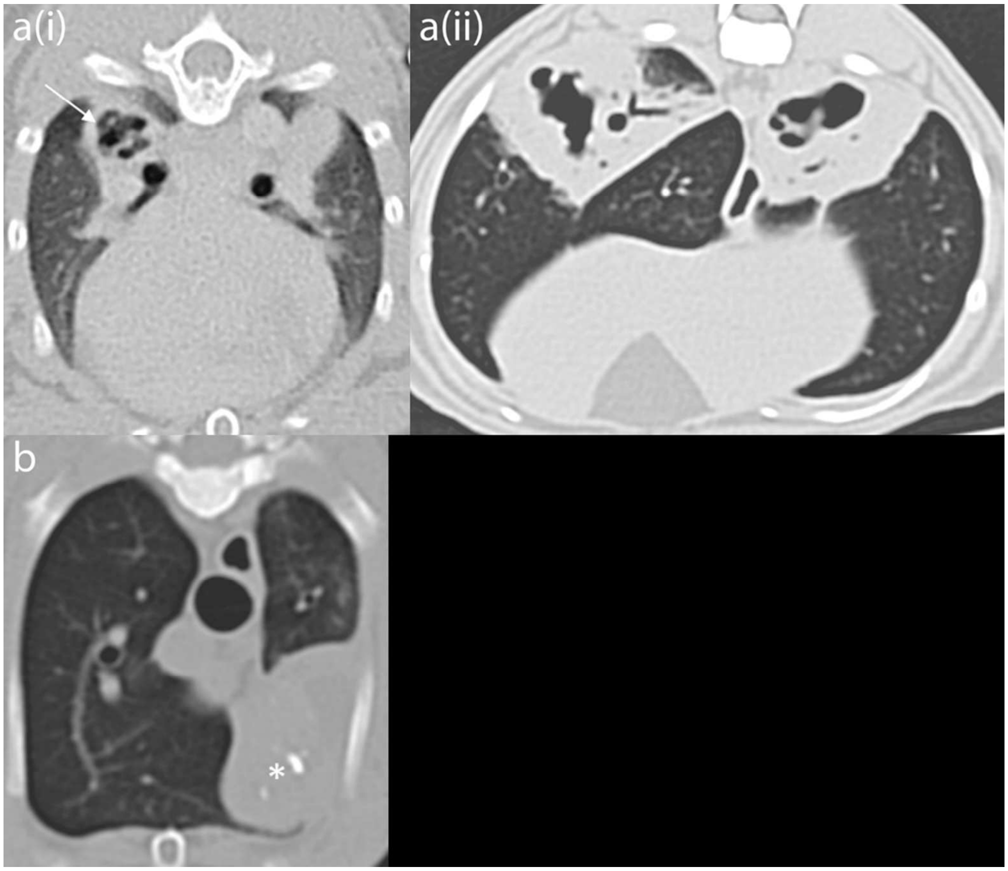

Figure 3. Less common thoracic abnormalities in three cats with mycobacteriosis. (a(i)) Transverse thoracic CT image at the level of the caudal mainstem bronchi showing a partially cavitated nodule (arrow). (a(ii)) Transverse thoracic CT image at the level of the accessory lung lobe showing more extensive parenchymal cavitation (b) Transverse thoracic CT image at the level of the third thoracic vertebra showing a region of alveolar pattern containing mineralised foci (*)
98x84mm (300 x 300 DPI)

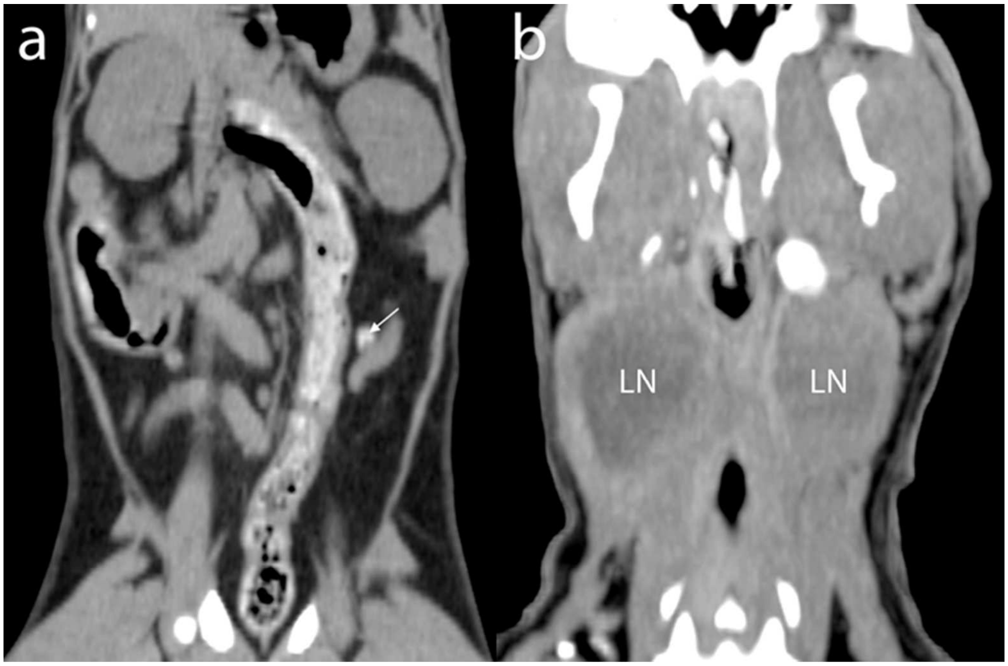

Figure 4. Extrathoracic lymphadenomegaly in two cats with mycobacteriosis. (a) Dorsal plane CT reconstruction of the abdomen at the level of the descending colon in a cat with a partially mineralised colic lymph node (arrow). (b) Dorsal plane CT reconstruction of the ventral neck in a cat with marked bilateral medial retropharyngeal lymphadenomegaly (LN)
128x84mm (300 x 300 DPI)

Figure 5. Bony lesions in four cats with mycobacteriosis. (a) Transverse CT image at the level of the canine teeth, demonstrating focal lysis (arrowhead) and moderate, irregular periosteal reaction (arrow). These is a soft tissue mass lesion associated with the bony change (*). (b) Transverse CT image at the level of the proximal radius and ulna which shows focal cortical lysis of the ulna (arrows) and marked smooth periosteal reaction. The adjacent radius is normal. (c) Sagittal plane CT reconstruction of the radius and ulna in a cat with a pathological fracture secondary to a tuberculous lesion. Lytic foci are visible in the distal radius (arrows), and there is a moderate smooth periosteal reaction (arrowhead). The adjacent ulna is normal. (d) Transverse CT image at the level of the humeral condyle showing marked periarticular new bone formation in a cat with a mycobacterial polyarthritis
152x140mm (300 x 300 DPI)

Figure 1. CT appearance of lung parenchyma in three cats with mycobacteriosis, at the level of the accessory lung lobe. (a) Alveolar pattern affecting multiple lung lobes. (b) Diffuse structured interstitial pattern comprising multiple relatively well defined nodules (arrows). (c) Diffuse structured interstitial pattern comprising mixed nodular and linear structures, characteristic of a reticulonodular pattern

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Computed Tomographic Findings in Cats with Mycobacterial Infection

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Keywords – feline, mycobacteriosis, computed tomography, infection, diagnosis

Abstract

Objectives

The objective of this study was to describe the imaging findings in computed tomography (CT) associated with confirmed mycobacterial infection in cats.

Methods

CT images from 20 cats with confirmed mycobacterial disease were retrospectively reviewed. Five cats underwent conscious full-body CT in a VetMouseTrap™ device. All other cats had thoracic CT performed under general anaesthesia, with the addition of CT investigation of the head/neck, abdomen and limbs in some cases.

Results

Mycobacterial infection was seen most frequently in adult (mean age 7.4 years; range 0.6-14 years) neutered male cats (11/20). The most common infections were *Mycobacterium microti* (6/20) and *Mycobacterium bovis* (6/20). CT abnormalities were most commonly seen in the thorax, consisting of bronchial (9/20), alveolar (8/20), ground glass (6/20) or structured interstitial (15/20) lung patterns, which were often mixed. Tracheobronchial, sternal and cranial mediastinal lymphadenomegaly were common (16/20). Other abnormalities included abdominal (8/13) or peripheral (10/18) lymphadenomegaly, hepatosplenomegaly (7/13), mixed osteolytic/osteoproliferative skeletal lesions (7/20), and cutaneous or subcutaneous soft tissue masses/nodules (4/20).

Conclusions and relevance

CT of feline mycobacteriosis shows a wide range of abnormalities often involving multiple organ systems and mimicking many other feline diseases. Mycobacteriosis

should be considered in the differential diagnosis of thoracic, abdominal and skeletal disorders in cats.

Introduction

Feline mycobacteriosis is a worldwide veterinary health concern, and although definitive data on case numbers worldwide are lacking, mycobacterial infections in cats have been recognised with increasing frequency in the UK, as well as being seen in many other countries. Mycobacterial disease in domestic cats can result from infection by one of a number of species. The most commonly identified mycobacteria include *Mycobacterium microti* and *Mycobacterium bovis*, which are primary pathogens and members of the tuberculous complex group of mycobacteria.[1-3] Non-tuberculous mycobacterial species are less commonly identified within clinically affected cats.[4]

Clinical presentation of mycobacterial infection in cats is variable, and is dependant primarily on the species of mycobacteria involved and, importantly, the route of infection.[2,5-7] Historically, alimentary lesions resulting from ingestion of milk from cows infected with *M. bovis* were most common; however with overall reduction of tuberculosis in the national bovine herd since the early 1900's and widespread pasteurisation of milk this is no longer the case.[8] Single or multiple cutaneous lesions with or without lymph node involvement, and characteristically affecting the so-called 'fight and bite sites' (such as the head and limbs), now represent the most common presentation of mycobacterial infection in cats: they typically result from infection acquired from prey species.[3,9] Infection acquired through inhalation or ingestion, resulting in respiratory or alimentary disease, is seen less frequently. The clinical presentation of these forms of disease, and of disseminated disease resulting from haematogenous spread of infection, can include non-specific signs such as weight loss, anorexia, coughing, anaemia, vomiting/diarrhoea, hepatosplenomegaly, generalised lymphadenopathy and pyrexia.[7]

Definitive diagnosis of mycobacterial disease in cats can present significant problems, in part due to difficulties in sample handling, and limitations in the available laboratory diagnostic techniques. As such, mycobacterial infections are likely underdiagnosed within the domestic cat population. In addition to significant morbidity resulting from primary infection, subclinical infection and recurrence of infection following treatment are common.[7] Since significant and potentially fatal multisystemic disease can result from infection with mycobacterial species, and since there are potential zoonotic risks associated with all members of the tuberculosis complex,[7,10] identification and correct handling of potential cases is of the upmost importance.

Previous publications detailing the diagnostic imaging findings in cats with confirmed mycobacterial infection are limited to a single retrospective case series looking at survey radiographic changes involving 33 cats,[11] and a number of isolated case reports describing the radiographic features of feline mycobacteriosis.[12-14] Computed tomography is increasingly available to the veterinary community, and it offers significant advantages over survey radiography by eliminating superimposition of anatomy, having superior contrast resolution and being able to clarify intrathoracic lesions where radiographic findings are negative or non-specific.[15,16] In addition, the decreased scan times which are achievable with modern multi-detector scanners make CT a valuable tool in investigation of multisystemic disease in clinically compromised patients. The CT features of mycobacterial disease in cats have not been described previously. The aim of this paper was to review CT images from a large number of cats with confirmed mycobacteriosis and to describe the range of abnormalities that can occur.

Materials and Methods

This study comprises a descriptive, retrospective case series. CT studies carried out between August 2009 and January 2015, of cats with confirmed mycobacterial infection were submitted to one of the authors (DGM). Inclusion criteria consisted of: (i) confirmation of mycobacterial infection and (ii) a CT study of diagnostic quality. To confirm mycobacterial involvement, aspirated and/or biopsy samples of affected tissue had been stained with Ziehl-Neelson (ZN) and found to have changes indicative of mycobacteriosis.[1] Where possible, tissue culture,[17] interferon-gamma release assay, or PCR testing had been used to identify which mycobacterial species was involved.[4,18,19]

Pseudonymised CT studies of the confirmed mycobacterial cases were examined without knowledge of specific clinical information by a third year diagnostic imaging resident who was however informed about the topic of the study (AM). To prevent bias by the assumption of disease, CT studies covering the thorax and other body parts from an additional ten cats with confirmed non-mycobacterial diseases were included and also pseudonymised. Images were evaluated using dedicated DICOM viewer software (Osirix, Geneva, Switzerland, version 5.8.5-64bit) on a computer workstation (Apple Mac Pro, Apple, USA) with a calibrated LCD flat screen monitor (Apple Cinemax Display, 30 inch, Apple, USA).

During the course of image evaluation, multi-planar reconstructions, maximum and minimum intensity projections and variable windowing settings were used according to the preferences of the viewer.

CT studies were reviewed for the following diagnostic criteria: bronchial thickening; alveolar pattern; ground glass opacity or structured interstitial lung change; evidence of pleural or pericardial effusion, or pleural/mediastinal thickening; thoracic, abdominal or peripheral lymphadenomegaly, or lymph node mineralisation; abdominal organomegaly, peritoneal effusion, other abdominal organ-associated lesions; osteolysis or osteoproliferative changes; cutaneous/subcutaneous/oral/nasal lesions; vascular and dystrophic soft tissue calcification. The extent of any abnormality was characterised as focal, multifocal, or diffuse. The degree of each change was graded as absent/normal, mild, moderate or severe.

Results

Twenty cats met the inclusion criteria. After all image interpretive data had been collected the additional ten non-mycobacterial cat studies were identified and their data were excluded from further analysis. The most common infections were *M. microti* and *M. bovis*, confirmed in 6/20 cases each. A non-specified *M. tuberculosis* complex species was described in one case and in the remaining 7/20 cases the species involved was not known. Eleven of the 20 cats were neutered males and 9/20 were neutered females. The study group comprised 7/20 Domestic Short Hair, 4/20 Siamese, 2/20 Domestic Long Hair and 1/20 of each of the following; Persian, Birman, Norwegian Forest Cat, Burmilla, British Short Hair, Bengal and Maine Coon cats. The age of one cat was not known. For the remaining cats the mean age was 7.4 ± 3.8 years (range 0.6-14 years).

Five of the 20 cats underwent conscious full-body CT in a specific containing device (VetMouseTrap™, University of Illinois at Urbana-Champaign, Urbana, IL).[20] The remaining 15 cats were scanned under general anaesthesia, with images of the following body regions obtained: thorax only (2), head/neck and thorax (3), thorax and abdomen (4), head/neck, thorax and abdomen (2), head/neck, thorax, abdomen and single forelimb (2), head, thorax, bilateral tarsi/elbows (1), thorax and single hind limb (1).

Intravenous contrast medium (iopamidol or iohexol, 600-700mg I/kg) was administered to 12/20 cats, and post-contrast images of some or all body parts were obtained. Use of contrast medium depended

on the findings in the pre-contrast images, the clinical condition of the cat, and the preferences of the attending radiologist and primary clinician in each case.

Within the evaluated imaging studies, thoracic abnormalities were noted in 19/20 cases. Diffuse bronchial thickening was present in 9/20 cats; being mild in eight cases and moderate in one. Eight cats showed a focal alveolar pattern; mild in two cases, moderate in three cases and severe in three cases (Figure 1(a)). Diffuse or patchy ground glass opacity was noted in 6/20 cats; mild in three cases, moderate in two cases and severe in one case. The most common pulmonary parenchymal change was a diffuse structured interstitial pattern, which was present in 15/20 cats, being either nodular (7/15) or reticulonodular (8/15) in nature; mild in six cases, moderate in five cases and severe in four cases (Figure 1(b,c)). Thoracic CT images of 14/20 cats were considered to show a mixed pulmonary pattern, with a single pattern present in 4/20 cases. The appearance of the pulmonary parenchyma was normal in 2/20 cats, though one of these had a thoracic lymphadenopathy despite normal lungs. Of the 20 cats, 16 had sternal, cranial mediastinal and/or tracheobronchial lymphadenomegaly (Figure 2). Moderate lymphadenomegaly affecting the sternal or tracheobronchial nodes was most common. One cat had moderate mineralisation of an enlarged cranial mediastinal lymph node.

None of the cats had any evidence of pleural or pericardial effusion. One cat showed mild, diffuse pleural thickening. One cat showed mild mineralisation of the aortic root. Two cats had regions of cavitation within the lungs, associated in both cases with focal or multifocal nodular or alveolar changes (Figure 3(a)). Three cats had scattered foci of mineralisation within the lungs, again associated with other focal parenchymal changes (Figure 3(b)).

Thirteen of the 20 cats had imaging studies that included the abdomen. Abdominal lymphadenomegaly was present in 8/13 cases and was typically generalised. The lymph nodes affected could not always be individually identified, but included those of the celiac and cranial mesenteric centres, which variably comprised the hepatic, splenic, gastric, pancreaticoduodenal, jejunal and colic nodes. Lymphadenomegaly was mild in two cats, moderate in four cats and severe in two cats. In one cat with a generalised moderate abdominal lymphadenomegaly, mild mineralisation of a mesenteric lymph node was present (Figure 4(a)). Mild hepatomegaly was present in 3/13 cats and moderate hepatomegaly in 1/13. Mild splenomegaly was present in 6/13 cats and moderate splenomegaly in 1/13. Two cats with

splenomegaly (one mild and one moderate) were also noted to show heterogeneity within the splenic parenchyma following contrast medium administration. Additional abdominal organ changes were noted in 3/13 cats; one had a moderately enlarged pancreas, one had multiple nodules within both kidneys, and one an irregular outline to the left kidney. Peritoneal effusion was not noted in any cat.

The appearance of the peripheral lymph nodes was assessed in 18/20 cats. The two cats not included in this assessment had CT studies of the thorax only, without inclusion of any extra-thoracic lymph node group. In 10/18 cases peripheral lymphadenomegaly was present, mild in 3/18, moderate in 2/18 and severe in 5/18. In 8/10 cats with lymphadenomegaly, the most significant enlargement was noted in the mandibular and medial retropharyngeal nodes (Figure 4(b)); however, multifocal lymphadenomegaly, involving the superficial cervical (prescapular), axillary, inguinal and/or popliteal nodes was variably present. In the other 2/10 cats, the head and neck were not imaged, but enlargement of the superficial cervical and popliteal lymph nodes was noted respectively. Five of the eight cats in which peripheral lymphadenomegaly was not noted underwent conscious CT in the VetMouseTrap™ device and three underwent CT studies which did not include the head and neck.

Focal osteolytic lesions were present in 7/20 cats (although it was not possible to assess the entire skeleton in 15 cats as they did not have full body CT examinations); changes were mild in four cases and moderate in three cases. These lesions affected the nasal bridge in three cats and the limbs in the remaining four, and were predominantly characterised by regions of cortical lysis (5/7) or erosive lesions at joint surfaces (2/7) (Figure 5). An associated pathological long bone fracture was present in one case. In all but one of these cases osteoproliferative changes, either periosteal reaction or periarticular osteophytosis, were noted in the same location as the osteolytic change. The osteoproliferation was mild in three cases and severe in three cases; however, the degree of proliferative change did not necessarily correlate with the degree of lytic change in each case.

Cutaneous or subcutaneous lesions were only infrequently present within the studies evaluated. Focal mass lesions over the nasal bridge were noted in 2/20 cats, graded moderate in one and severe in one. One other cat had a small amount of fluid accumulation and soft tissue thickening in the dorsal nasal chambers. Each of these lesions was adjacent to bony abnormalities. A focal, but extensive, mass lesion was noted along the ventral head and neck of one cat. One cat was found to have multiple, widely

distributed, subcutaneous nodules. Diffuse extra-thoracic dystrophic soft tissue mineralisation was not noted in any cat.

Discussion

Mycobacteriosis in cats is known to be a highly variable disease, and should always be considered as a possible differential diagnosis in cases which present with multisystemic signs. Mycobacterial disease is likely under-recognised, primarily due to a lack of awareness of the full spectrum of changes which can be associated with it.

Mycobacterial infection is most commonly seen in adult, neutered male cats consistent with the results of our study.[9] Domestic Short Hair cats predominate in our study, but to a lesser degree than noted in the previous radiographic case series (36% vs 87%).[11] The reason for this is unknown, but may reflect a higher proportion of pedigree cats within a referral population, which are therefore more likely to undergo advanced imaging.

CT abnormalities of the thorax were commonly noted, being present in all but one cat. However, multisystemic abnormalities were also common, with changes affecting more than one anatomical region in all but five cases. Of these five, three had abnormalities detected on clinical examination which were not appreciable on the CT images. In cats, systemic mycobacterial infection is most commonly caused by *M. bovis* or *M microti*,[3,9,21-24] and our results are consistent with this.

Previous reports of radiographic findings in cats with mycobacterial disease described a mild predominance of a mixed lung pattern (ie, a combination of bronchial, alveolar and/or interstitial changes),[1,9,11-13,22-24] but distinct alveolar, bronchial or interstitial patterns in isolation were also identified.[11] Interestingly, where cases in our study displayed mixed lung patterns, bronchial thickening and ground glass opacity were most commonly graded as mild, whereas alveolar pattern and structured interstitial patterns were more likely to be moderate or severe. This is interesting for two reasons. Firstly, the mild bronchial and unstructured interstitial patterns are of a degree that comparable changes may not be easily visible radiographically, or may be attributed to expiratory or underexposed radiographs, or superimposition of other structures. In a radiographic study it is therefore possible that only a more significant overlying alveolar or nodular pattern may be recognised, leading to classification as a single

lung pattern. As superimposition effects are eliminated by CT, it becomes easier to identify these mild changes in addition to the more marked ones. Secondly, a mild bronchial or unstructured interstitial pattern may be indicative of concurrent conditions, such as low-grade allergic airway disease, rather than being directly related to an active mycobacterial infection.[25,26] Differentiation of these may not be possible.

Within our study, the most commonly encountered single lung pattern was structured interstitial. However, these cases could be further subdivided into cases displaying a nodular pattern, comprising scattered rounded hyperattenuating foci, and a reticulonodular pattern, where rounded foci and linear or sickle-shaped hyperattenuating structures overlie to give a more complex overall pattern. In humans, a faint, diffuse reticulonodular pattern is considered characteristic of miliary tuberculosis.[27] While nodular and reticulonodular patterns are distinguishable on good quality radiographs in cats, the distinction is only rarely made in veterinary imaging. On CT however, the difference is more easily appreciable. The diagnostic and prognostic significance of the variable patterns in feline patients is currently unknown, but certainly warrants further investigation, as a structured interstitial pattern is a common finding in many feline lung pathologies (eg, pulmonary fibrosis, metastatic neoplasia, eosinophilic bronchopneumopathy and a wide range of infectious pneumonias).

It is interesting to note that within our study population, two cats were found to have cavitations within their lungs. While this feature is relatively common in both humans and dogs with tuberculosis[28-30] it was not noted in any case in the previous radiographic study of cats,[11] and the only paper which describes cavitating tubercles in cats was published in 1949.[5] The lesions noted in the two cats in this study were small (<1 cm) and were contained within regions of nodular or alveolar change. It is possible therefore that they may not have been visible on radiographs, again highlighting the advantage of cross sectional imaging. Alternatively, this may indeed reflect a rare occurrence in feline patients, which has occurred coincidentally within our study population. In either case, it is an important characteristic to recognise, as cavitated lung masses are occasionally identified in feline patients with lung neoplasia,[16,25] and the potential for misdiagnosis exists in cats with mycobacteriosis which show this feature. In addition this should be recognised because these cats likely pose an increased zoonotic risk compared with those showing the more typical structured interstitial pattern as they may allow mycobacteria to gain access to the upper airways.

Thoracic lymphadenomegaly is a feature of numerous pulmonary and multisystemic conditions in cats including, but not limited to, infiltrative and metastatic neoplasia, hypereosinophilic syndromes and systemic mycosis/bacteriosis.[31] As expected thoracic lymphadenomegaly was commonly noted within our study population, but in contrast to the findings of the previous radiographic paper, mild and moderate enlargement predominated over severe.[11] This may reflect the difficulty in recognising minor changes on radiographs. It is also worth noting that even given the superior contrast resolution of CT, with mild lymphadenomegaly, particularly in the perihilar region; changes were more easily appreciated in post-contrast studies when compared with pre-contrast. This suggests that there is value in performing post-contrast scans in all cases (unless there is a clinical contraindication), which was not standard practice within our study population.

Mineralisation of thoracic lymph nodes and pulmonary parenchyma can result from chronic inflammation associated with mycobacterial infection;[9,13,32] it is also seen in cases of both primary and metastatic pulmonary neoplasia, and chronic airways disease.[25] In either case, it is a finding which most likely relates to the disease process that is present. In contrast, mild aortic root calcification, such as that seen in one case (a seven year old cat) in our study is, in our experience, an occasional finding in middle aged to older cats, and not necessarily related to clinical disease.

While peripheral and abdominal lymphadenomegaly were relatively common within the study population, it is possible that the number of cases with mild or moderate lymphadenomegaly in the head and neck was artificially low. This is because all cases recorded as having normal peripheral lymph nodes on physical examination either did not undergo imaging of the head and neck, or were scanned conscious within a VetMouseTrap™ device. The protocol for these scans involved a short scan time (in order to minimise movement) resulting in a relatively large slice thickness and consequently a reduced longitudinal resolution. This can compromise assessment of small structures so it is possible that mild or moderate abnormalities of the head and neck, such as lymphadenomegaly, may have been overlooked. Other abdominal changes such as hepatomegaly, splenomegaly, renal and pancreatic changes were noted relatively infrequently and were mild or moderate in extent, consistent with previous reports.[9,11,12,33]

Two distinct manifestations of skeletal disease were noted within our population. The lesions characterised by cortical lysis likely represent sites of primary bacterial inoculation and as such are

consistent in location with 'fight and bite' injuries; whereas periarticular abnormalities are consistent with an infectious polyarthritis resulting from haematogenous dissemination of bacteria. It is interesting to note that the appendicular skeletal lesions in this study were clinically evident, and affected regions were intentionally included in the imaging studies. Clinically silent skeletal lesions may have been overlooked as the limbs were excluded from the majority of studies. The only studies in which the limbs were included in full were those performed using the VetMouseTrap™ device and it is possible that subtle or focal regions of bone lysis or proliferation may not have been recognised due to the lower resolution of these studies.

Cutaneous lesions were noted infrequently in this study. While this may initially seem surprising, given that cutaneous lesions represent a common presentation of mycobacteriosis,[3,9] it reflects the fact that CT imaging is more likely to be employed in cases presenting with systemic disease, or used as a staging tool in cats with clinically evident focal skin lesions without requirement for imaging of the lesions themselves. The presence of intranasal changes in one cat is interesting, as these are indicative of a mycobacterial rhinitis, a manifestation of respiratory mycobacteriosis which may not be commonly recognised.

There are a number of limitations to this study. The most significant of these is that although mycobacteriosis was confirmed in each case, histopathology on all involved tissues was not typically performed; therefore, it is not possible to confirm that all changes seen were due to mycobacterial infection. Due to the inherent difficulties in confirmation of mycobacterial infection, the time lapse between acquisition of CT images and definitive confirmation of diagnosis was very variable; it extended to four years and nine months in one case (though a lapse of one to four months was more typical). In all cases however, at the time of imaging, the combination of clinical and pathological findings gave sufficient confidence in the diagnosis to allow treatment to be instigated; imaging was used to stage the cases and so guide the intensity and duration of treatment. The evolution of changes over time in association with treatment has not been described, and will be interesting to explore in the future. Finally, given the retrospective nature of this study there are inconsistencies between cases with respect to factors such as regions imaged and use of contrast medium. This leads to a bias in our results, and may underestimate subclinical disease, particularly affecting the peripheral structures. As mentioned, the limited resolution of smaller structures on VetMouseTrap™ scans contributes to this. However, the advantages of this technique

for disease screening, particularly in clinically compromised patients should not be ignored, and as faster scanners become more commonplace many of the resolution difficulties will be eliminated.

Conclusions

As expected, the majority of CT changes noted in this study represent multisystemic disease, typically with combinations of pulmonary infiltration, lymphadenomegaly and organomegaly. These changes are strongly suggestive of infiltrative disease, differentials for which can include neoplasia (such as lymphoma or mast cell disease), chronic inflammation/infectious processes (mycobacteriosis, feline infectious peritonitis or systemic mycosis), hypereosinophilic syndrome and amyloidosis.[24] While no abnormality has been recognised that is specific for mycobacteriosis, it is important that the potential for mycobacterial infection is considered when these types of changes are identified in feline patients, especially if they have non-specific clinical signs. In addition, when managing patients with a diagnosis of mycobacteriosis, the potential for widespread clinical and sub-clinical abnormalities must be considered and investigated in full.

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Figure 1. CT appearance of lung parenchyma in three cats with mycobacteriosis, at the level of the accessory lung lobe. (a) Alveolar pattern affecting multiple lung lobes. (b) Diffuse structured interstitial pattern comprising multiple relatively well defined nodules (arrows). (c) Diffuse structured interstitial pattern comprising mixed nodular and linear structures, characteristic of a reticulonodular pattern

Figure 2. Thoracic lymphadenopathy in two cats with mycobacteriosis. (a) Transverse thoracic CT image at the level of the third sternebra showing an enlarged cranial mediastinal lymph node (arrowheads) containing a focus of mineralisation (arrow). (b) Post-contrast transverse CT image at the level of the cardiac base showing bilaterally enlarged tracheobronchial lymph nodes (LN) surrounding the trachea (T). The use of contrast medium allows differentiation from the cardiac and vascular structures

Figure 3. Less common thoracic abnormalities in three cats with mycobacteriosis. (a(i)) Transverse thoracic CT image at the level of the caudal mainstem bronchi showing a partially cavitated nodule (arrow). (a(ii)) Transverse thoracic CT image at the level of the accessory lung lobe showing more extensive parenchymal cavitation (b) Transverse thoracic CT image at the level of the third thoracic vertebra showing a region of alveolar pattern containing mineralised foci (*)

Figure 4. Extrathoracic lymphadenomegaly in two cats with mycobacteriosis. (a) Dorsal plane CT reconstruction of the abdomen at the level of the descending colon in a cat with a partially mineralised colic lymph node (arrow). (b) Dorsal plane CT reconstruction of the ventral neck in a cat with marked bilateral medial retropharyngeal lymphadenomegaly (LN)

Figure 5. Bony lesions in four cats with mycobacteriosis. (a) Transverse CT image at the level of the canine teeth, demonstrating focal lysis (arrowhead) and moderate, irregular periosteal reaction (arrow). These is a soft tissue mass lesion associated with the bony change (*). (b) Transverse CT image at the level of the proximal radius and ulna which shows focal cortical lysis of the ulna (arrows) and marked smooth periosteal reaction. The adjacent radius is normal. (c) Sagittal plane CT reconstruction of the radius and ulna in a cat with a pathological fracture secondary to a tuberculous lesion. Lytic foci are visible in the distal radius (arrows), and there is a moderate smooth periosteal reaction (arrowhead). The adjacent ulna is normal. (d) Transverse CT image at the level of the humeral condyle showing marked periarticular new bone formation in a cat with a mycobacterial polyarthritis