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Computed Tomographic Findings in Cats with Mycobacterial Infection

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Journal:	*Journal of Feline Medicine and Surgery*
Manuscript ID:	JFMS-15-0032.R1
Manuscript Type:	Original Article
Date Submitted by the Author:	06-May-2015
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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 VetMouseTrapTM 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. |
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1   **Computed Tomographic Findings in Cats with Mycobacterial Infection**

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24   **Abstract**

25

26   **Objectives**

27   The objective of this study was to describe the imaging findings in computed tomography

28   (CT) associated with confirmed mycobacterial infection in cats.

29   **Methods**

30   CT images from 20 cats with confirmed mycobacterial disease were retrospectively

31   reviewed. Five cats underwent conscious full-body CT in a VetMouseTrap[TM] device. All

32   other cats had thoracic CT performed under general anaesthesia, with the addition of CT

33   investigation of the head/neck, abdomen and limbs in some cases.

34   **Results**

35   Mycobacterial infection was seen most frequently in adult (mean age 7.4 years; range

36   0.6-14 years) neutered male cats (11/20). The most common infections were

37   *Mycobacterium microti* (6/20) and *Mycobacterium bovis* (6/20). CT abnormalities were

38   most commonly seen in the thorax, consisting of bronchial (9/20), alveolar (8/20), ground

39   glass (6/20) or structured interstitial (15/20) lung patterns, which were often mixed.

40   Tracheobronchial, sternal and cranial mediastinal lymphadenomegaly were common

41   (16/20). Other abnormalities included abdominal (8/13) or peripheral (10/18)

42   lymphadenomegaly, hepatosplenomegaly (7/13), mixed osteolytic/osteoproliferative

43   skeletal lesions (7/20), and cutaneous or subcutaneous soft tissue masses/nodules (4/20).

44   **Conclusions and relevance**

45   CT of feline mycobacteriosis shows a wide range of abnormalities often involving

46   multiple organ systems and mimicking many other feline diseases. Mycobacteriosis

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47   should be considered in the differential diagnosis of thoracic, abdominal and skeletal

48   disorders in cats.

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Introduction

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53   Feline mycobacteriosis is a worldwide veterinary health concern, and although definitive data on

54   case numbers worldwide are lacking, mycobacterial infections in cats have been recognised with increasing

55   frequency in the UK, as well as being seen in many other countries. Mycobacterial disease in domestic cats

56   can result from infection by one of a number of species. The most commonly identified mycobacteria

57   include *Mycobacterium microti* and *Mycobacterium bovis*, which are primary pathogens and members of

58   the tuberculous complex group of mycobacteria.[1-3] Non-tuberculous mycobacterial species are less

59   commonly identified within clinically affected cats.[4]

60   Clinical presentation of mycobacterial infection in cats is variable, and is dependant primarily on

61   the species of mycobacteria involved and, importantly, the route of infection.[2,5-7] Historically, alimentary

62   lesions resulting from ingestion of milk from cows infected with *M. bovis* were most common; however

63   with overall reduction of tuberculosis in the national bovine herd since the early 1900's and widespread

64   pasteurisation of milk this is no longer the case.[8] Single or multiple cutaneous lesions with or without

65   lymph node involvement, and characteristically affecting the so-called 'fight and bite sites' (such as the

66   head and limbs), now represent the most common presentation of mycobacterial infection in cats: they

67   typically result from infection acquired from prey species.[3,9] Infection acquired through inhalation or

68   ingestion, resulting in respiratory or alimentary disease, is seen less frequently. The clinical presentation of

69   these forms of disease, and of disseminated disease resulting from haematogenous spread of infection, can

70   include non-specific signs such as weight loss, anorexia, coughing, anaemia, vomiting/diarrhoea,

71   hepatosplenomegaly, generalised lymphadenopathy and pyrexia.[7]

72   Definitive diagnosis of mycobacterial disease in cats can present significant problems, in part due

73   to difficulties in sample handling, and limitations in the available laboratory diagnostic techniques. As

74   such, mycobacterial infections are likely underdiagnosed within the domestic cat population. In addition to

75   significant morbidity resulting from primary infection, subclinical infection and recurrence of infection

76   following treatment are common.[7] Since significant and potentially fatal multisystemic disease can result

77   from infection with mycobacterial species, and since there are potential zoonotic risks associated with all

78   members of the tuberculosis complex,[7,10] identification and correct handling of potential cases is of the

79   upmost importance.

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80   Previous publications detailing the diagnostic imaging findings in cats with confirmed

81   mycobacterial infection are limited to a single retrospective case series looking at survey radiographic

82   changes involving 33 cats,[11] and a number of isolated case reports describing the radiographic features of

83   feline mycobacteriosis.[12-14] Computed tomography is increasingly available to the veterinary community,

84   and it offers significant advantages over survey radiography by eliminating superimposition of anatomy,

85   having superior contrast resolution and being able to clarify intrathoracic lesions where radiographic

86   findings are negative or non-specific.[15,16] In addition, the decreased scan times which are achievable with

87   modern multi-detector scanners make CT a valuable tool in investigation of multisystemic disease in

88   clinically compromised patients. The CT features of mycobacterial disease in cats have not been described

89   previously. The aim of this paper was to review CT images from a large number of cats with confirmed

90   mycobacteriosis and to describe the range of abnormalities that can occur.

91

92   **Materials and Methods**

93   This study comprises a descriptive, retrospective case series. CT studies carried out between

94   August 2009 and January 2015, of cats with confirmed mycobacterial infection were submitted to one of

95   the authors (DGM). Inclusion criteria consisted of: (i) confirmation of mycobacterial infection and (ii) a CT

96   study of diagnostic quality. To confirm mycobacterial involvement, aspirated and/or biopsy samples of

97   affected tissue had been stained with Ziehl-Neelson (ZN) and found to have changes indicative of

98   mycobacteriosis.[1] Where possible, tissue culture,[17] interferon-gamma release assay, or PCR testing had

99   been used to identify which mycobacterial species was involved.[4,18,19]

100   Pseudonymised CT studies of the confirmed mycobacterial cases were examined without

101   knowledge of specific clinical information by a third year diagnostic imaging resident who was however

102   informed about the topic of the study (AM). To prevent bias by the assumption of disease, CT studies

103   covering the thorax and other body parts from an additional ten cats with confirmed non-mycobacterial

104   diseases were included and also pseudonymised. Images were evaluated using dedicated DICOM viewer

105   software (Osirix, Geneva, Switzerland, version 5.8.5-64bit) on a computer workstation (Apple Mac Pro,

106   Apple, USA) with a calibrated LCD flat screen monitor (Apple Cinemax Display, 30 inch, Apple, USA).

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107   During the course of image evaluation, multi-planar reconstructions, maximum and minimum intensity

108   projections and variable windowing settings were used according to the preferences of the viewer.

109   CT studies were reviewed for the following diagnostic criteria: bronchial thickening; alveolar

110   pattern; ground glass opacity or structured interstitial lung change; evidence of pleural or pericardial

111   effusion, or pleural/mediastinal thickening; thoracic, abdominal or peripheral lymphadenomegaly, or lymph

112   node mineralisation; abdominal organomegaly, peritoneal effusion, other abdominal organ-associated

113   lesions; osteolysis or osteoproliferative changes; cutaneous/subcutaneous/oral/nasal lesions; vascular and

114   dystrophic soft tissue calcification. The extent of any abnormality was characterised as focal, multifocal, or

115   diffuse. The degree of each change was graded as absent/normal, mild, moderate or severe.

116

117   **Results**

118   Twenty cats met the inclusion criteria. After all image interpretive data had been collected the

119   additional ten non-mycobacterial cat studies were identified and their data were excluded from further

120   analysis. The most common infections were *M. microti* and *M. bovis*, confirmed in 6/20 cases each. A non-

121   specified *M. tuberculosis* complex species was described in one case and in the remaining 7/20 cases the

122   species involved was not known. Eleven of the 20 cats were neutered males and 9/20 were neutered

123   females. The study group comprised 7/20 Domestic Short Hair, 4/20 Siamese, 2/20 Domestic Long Hair

124   and 1/20 of each of the following; Persian, Birman, Norwegian Forest Cat, Burmilla, British Short Hair,

125   Bengal and Maine Coon cats. The age of one cat was not known. For the remaining cats the mean age was

126   7.4 ± 3.8 years (range 0.6-14 years).

127   Five of the 20 cats underwent conscious full-body CT in a specific containing device

128   (VetMouseTrap™, University of Illinois at Urbana-Champaign, Urbana, IL).[20] The remaining 15 cats were

129   scanned under general anaesthesia, with images of the following body regions obtained: thorax only (2),

130   head/neck and thorax (3), thorax and abdomen (4), head/neck, thorax and abdomen (2), head/neck, thorax,

131   abdomen and single forelimb (2), head, thorax, bilateral tarsi/elbows (1), thorax and single hind limb (1).

132   Intravenous contrast medium (iopamidol or iohexol, 600-700mg I/kg) was administered to 12/20

133   cats, and post-contrast images of some or all body parts were obtained. Use of contrast medium depended

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134   on the findings in the pre-contrast images, the clinical condition of the cat, and the preferences of the

135   attending radiologist and primary clinician in each case.

136   　　　Within the evaluated imaging studies, thoracic abnormalities were noted in 19/20 cases. Diffuse

137   bronchial thickening was present in 9/20 cats; being mild in eight cases and moderate in one. Eight cats

138   showed a focal alveolar pattern; mild in two cases, moderate in three cases and severe in three cases (Figure

139   1(a)). Diffuse or patchy ground glass opacity was noted in 6/20 cats; mild in three cases, moderate in two

140   cases and severe in one case. The most common pulmonary parenchymal change was a diffuse structured

141   interstitial pattern, which was present in 15/20 cats, being either nodular (7/15) or reticulonodular (8/15) in

142   nature; mild in six cases, moderate in five cases and severe in four cases (Figure 1(b,c)). Thoracic CT

143   images of 14/20 cats were considered to show a mixed pulmonary pattern, with a single pattern present in

144   4/20 cases. The appearance of the pulmonary parenchyma was normal in 2/20 cats, though one of these had

145   a thoracic lymphadenopathy despite normal lungs. Of the 20 cats, 16 had sternal, cranial mediastinal and/or

146   tracheobronchial lymphadenomegaly (Figure 2). Moderate lymphadenomegaly affecting the sternal or

147   tracheobronchial nodes was most common. One cat had moderate mineralisation of an enlarged cranial

148   mediastinal lymph node.

149   　　　None of the cats had any evidence of pleural or pericardial effusion. One cat showed mild, diffuse

150   pleural thickening. One cat showed mild mineralisation of the aortic root. Two cats had regions of

151   cavitation within the lungs, associated in both cases with focal or multifocal nodular or alveolar changes

152   (Figure 3(a)). Three cats had scattered foci of mineralisation within the lungs, again associated with other

153   focal parenchymal changes (Figure 3(b)).

154   　　　Thirteen of the 20 cats had imaging studies that included the abdomen. Abdominal

155   lymphadenomegaly was present in 8/13 cases and was typically generalised. The lymph nodes affected

156   could not always be individually identified, but included those of the celiac and cranial mesenteric centres,

157   which variably comprised the hepatic, splenic, gastric, pancreaticoduodenal, jejunal and colic nodes.

158   Lymphadenomegaly was mild in two cats, moderate in four cats and severe in two cats. In one cat with a

159   generalised moderate abdominal lymphadenomegaly, mild mineralisation of a mesenteric lymph node was

160   present (Figure 4(a)). Mild hepatomegaly was present in 3/13 cats and moderate hepatomegaly in 1/13.

161   Mild splenomegaly was present in 6/13 cats and moderate splenomegaly in 1/13. Two cats with

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162 splenomegaly (one mild and one moderate) were also noted to show heterogeneity within the splenic

163 parenchyma following contrast medium administration. Additional abdominal organ changes were noted in

164 3/13 cats; one had a moderately enlarged pancreas, one had multiple nodules within both kidneys, and one

165 an irregular outline to the left kidney. Peritoneal effusion was not noted in any cat.

166 The appearance of the peripheral lymph nodes was assessed in 18/20 cats. The two cats not

167 included in this assessment had CT studies of the thorax only, without inclusion of any extra-thoracic

168 lymph node group. In 10/18 cases peripheral lymphadenomegaly was present, mild in 3/18, moderate in

169 2/18 and severe in 5/18. In 8/10 cats with lymphadenomegaly, the most significant enlargement was noted

170 in the mandibular and medial retropharyngeal nodes (Figure 4(b)); however, multifocal

171 lymphadenomegaly, involving the superficial cervical (prescapular), axillary, inguinal and/or popliteal

172 nodes was variably present. In the other 2/10 cats, the head and neck were not imaged, but enlargement of

173 the superficial cervical and popliteal lymph nodes was noted respectively. Five of the eight cats in which

174 peripheral lymphadenomegaly was not noted underwent conscious CT in the VetMouseTrap™ device and

175 three underwent CT studies which did not include the head and neck.

176 Focal osteolytic lesions were present in 7/20 cats (although it was not possible to assess the entire

177 skeleton in 15 cats as they did not have full body CT examinations); changes were mild in four cases and

178 moderate in three cases. These lesions affected the nasal bridge in three cats and the limbs in the remaining

179 four, and were predominantly characterised by regions of cortical lysis (5/7) or erosive lesions at joint

180 surfaces (2/7) (Figure 5). An associated pathological long bone fracture was present in one case. In all but

181 one of these cases osteoproliferative changes, either periosteal reaction or periarticular osteophytosis, were

182 noted in the same location as the osteolytic change. The osteoproliferation was mild in three cases and

183 severe in three cases; however, the degree of proliferative change did not necessarily correlate with the

184 degree of lytic change in each case.

185 Cutaneous or subcutaneous lesions were only infrequently present within the studies evaluated.

186 Focal mass lesions over the nasal bridge were noted in 2/20 cats, graded moderate in one and severe in one.

187 One other cat had a small amount of fluid accumulation and soft tissue thickening in the dorsal nasal

188 chambers. Each of these lesions was adjacent to bony abnormalities. A focal, but extensive, mass lesion

189 was noted along the ventral head and neck of one cat. One cat was found to have multiple, widely

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190 distributed, subcutaneous nodules. Diffuse extra-thoracic dystrophic soft tissue mineralisation was not

191 noted in any cat.

192

193 **Discussion**

194   Mycobacteriosis in cats is known to be a highly variable disease, and should always be considered

195 as a possible differential diagnosis in cases which present with multisystemic signs. Mycobacterial disease

196 is likely under-recognised, primarily due to a lack of awareness of the full spectrum of changes which can

197 be associated with it.

198   Mycobacterial infection is most commonly seen in adult, neutered male cats consistent with the

199 results of our study.[9] Domestic Short Hair cats predominate in our study, but to a lesser degree than noted

200 in the previous radiographic case series (36% vs 87%).[11] The reason for this is unknown, but may reflect a

201 higher proportion of pedigree cats within a referral population, which are therefore more likely to undergo

202 advanced imaging.

203   CT abnormalities of the thorax were commonly noted, being present in all but one cat. However,

204 multisystemic abnormalities were also common, with changes affecting more than one anatomical region in

205 all but five cases. Of these five, three had abnormalities detected on clinical examination which were not

206 appreciable on the CT images. In cats, systemic mycobacterial infection is most commonly caused by *M.*

207 *bovis* or *M microti*,[3,9,21-24] and our results are consistent with this.

208   Previous reports of radiographic findings in cats with mycobacterial disease described a mild

209 predominance of a mixed lung pattern (ie, a combination of bronchial, alveolar and/or interstitial

210 changes),[1,9,11-13,22-24] but distinct alveolar, bronchial or interstitial patterns in isolation were also identified.[11]

211 Interestingly, where cases in our study displayed mixed lung patterns, bronchial thickening and ground

212 glass opacity were most commonly graded as mild, whereas alveolar pattern and structured interstitial

213 patterns were more likely to be moderate or severe. This is interesting for two reasons. Firstly, the mild

214 bronchial and unstructured interstitial patterns are of a degree that comparable changes may not be easily

215 visible radiographically, or may be attributed to expiratory or underexposed radiographs, or

216 superimposition of other structures. In a radiographic study it is therefore possible that only a more

217 significant overlying alveolar or nodular pattern may be recognised, leading to classification as a single

9

218 lung pattern. As superimposition effects are eliminated by CT, it becomes easier to identify these mild

219 changes in addition to the more marked ones. Secondly, a mild bronchial or unstructured interstitial pattern

220 may be indicative of concurrent conditions, such as low-grade allergic airway disease, rather than being

221 directly related to an active mycobacterial infection.[25,26] Differentiation of these may not be possible.

222   Within our study, the most commonly encountered single lung pattern was structured interstitial.

223 However, these cases could be further subdivided into cases displaying a nodular pattern, comprising

224 scattered rounded hyperattenuating foci, and a reticulonodular pattern, where rounded foci and linear or

225 sickle-shaped hyperattenuating structures overlie to give a more complex overall pattern. In humans, a

226 faint, diffuse reticulonodular pattern is considered characteristic of miliary tuberculosis.[27] While nodular

227 and reticulonodular patterns are distinguishable on good quality radiographs in cats, the distinction is only

228 rarely made in veterinary imaging. On CT however, the difference is more easily appreciable. The

229 diagnostic and prognostic significance of the variable patterns in feline patients is currently unknown, but

230 certainly warrants further investigation, as a structured interstitial pattern is a common finding in many

231 feline lung pathologies (eg, pulmonary fibrosis, metastatic neoplasia, eosinophilic bronchopneumopathy

232 and a wide range of infectious pneumonias).

233   It is interesting to note that within our study population, two cats were found to have cavitations

234 within their lungs. While this feature is relatively common in both humans and dogs with tuberculosis[28-30] it

235 was not noted in any case in the previous radiographic study of cats,[11] and the only paper which describes

236 cavitating tubercles in cats was published in 1949.[5] The lesions noted in the two cats in this study were

237 small (<1 cm) and were contained within regions of nodular or alveolar change. It is possible therefore that

238 they may not have been visible on radiographs, again highlighting the advantage of cross sectional imaging.

239 Alternatively, this may indeed reflect a rare occurrence in feline patients, which has occurred coincidentally

240 within our study population. In either case, it is an important characteristic to recognise, as cavitated lung

241 masses are occasionally identified in feline patients with lung neoplasia,[16,25] and the potential for

242 misdiagnosis exists in cats with mycobacteriosis which show this feature. In addition this should be

243 recognised because these cats likely pose an increased zoonotic risk compared with those showing the more

244 typical structured interstitial pattern as they may allow mycobacteria to gain access to the upper airways.

245   Thoracic lymphadenomegaly is a feature of numerous pulmonary and multisystemic conditions in

246   cats including, but not limited to, infiltrative and metastatic neoplasia, hypereosinophilic syndromes and

247   systemic mycosis/bacteriosis.[31] As expected thoracic lymphadenomegaly was commonly noted within our

248   study population, but in contrast to the findings of the previous radiographic paper, mild and moderate

249   enlargement predominated over severe.[11] This may reflect the difficulty in recognising minor changes on

250   radiographs. It is also worth noting that even given the superior contrast resolution of CT, with mild

251   lymphadenomegaly, particularly in the perihilar region; changes were more easily appreciated in post-

252   contrast studies when compared with pre-contrast. This suggests that there is value in performing post-

253   contrast scans in all cases (unless there is a clinical contraindication), which was not standard practice

254   within our study population.

255   Mineralisation of thoracic lymph nodes and pulmonary parenchyma can result from chronic

256   inflammation associated with mycobacterial infection;[9,13,32] it is also seen in cases of both primary and

257   metastatic pulmonary neoplasia, and chronic airways disease.[25] In either case, it is a finding which most

258   likely relates to the disease process that is present. In contrast, mild aortic root calcification, such as that

259   seen in one case (a seven year old cat) in our study is, in our experience, an occasional finding in middle

260   aged to older cats, and not necessarily related to clinical disease.

261   While peripheral and abdominal lymphadenomegaly were relatively common within the study

262   population, it is possible that the number of cases with mild or moderate lymphadenomegaly in the head

263   and neck was artificially low. This is because all cases recorded as having normal peripheral lymph nodes

264   on physical examination either did not undergo imaging of the head and neck, or were scanned conscious

265   within a VetMouseTrap[TM] device. The protocol for these scans involved a short scan time (in order to

266   minimise movement) resulting in a relatively large slice thickness and consequently a reduced longitudinal

267   resolution. This can compromise assessment of small structures so it is possible that mild or moderate

268   abnormalities of the head and neck, such as lymphadenomegaly, may have been overlooked. Other

269   abdominal changes such as hepatomegaly, splenomegaly, renal and pancreatic changes were noted

270   relatively infrequently and were mild or moderate in extent, consistent with previous reports.[9,11,12,33]

271   Two distinct manifestations of skeletal disease were noted within our population. The lesions

272   characterised by cortical lysis likely represent sites of primary bacterial inoculation and as such are

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273   consistent in location with 'fight and bite' injuries; whereas periarticular abnormalities are consistent with

274   an infectious polyarthritis resulting from haematogenous dissemination of bacteria. It is interesting to note

275   that the appendicular skeletal lesions in this study were clinically evident, and affected regions were

276   intentionally included in the imaging studies. Clinically silent skeletal lesions may have been overlooked as

277   the limbs were excluded from the majority of studies. The only studies in which the limbs were included in

278   full were those performed using the VetMouseTrap™ device and it is possible that subtle or focal regions

279   of bone lysis or proliferation may not have been recognised due to the lower resolution of these studies.

280   Cutaneous lesions were noted infrequently in this study. While this may initially seem surprising,

281   given that cutaneous lesions represent a common presentation of mycobacteriosis,[3,9] it reflects the fact that

282   CT imaging is more likely to be employed in cases presenting with systemic disease, or used as a staging

283   tool in cats with clinically evident focal skin lesions without requirement for imaging of the lesions

284   themselves. The presence of intranasal changes in one cat is interesting, as these are indicative of a

285   mycobacterial rhinitis, a manifestation of respiratory mycobacteriosis which may not be commonly

286   recognised.

287   There are a number of limitations to this study. The most significant of these is that although

288   mycobacteriosis was confirmed in each case, histopathology on all involved tissues was not typically

289   performed; therefore, it is not possible to confirm that all changes seen were due to mycobacterial infection.

290   Due to the inherent difficulties in confirmation of mycobacterial infection, the time lapse between

291   acquisition of CT images and definitive confirmation of diagnosis was very variable; it extended to four

292   years and nine months in one case (though a lapse of one to four months was more typical). In all cases

293   however, at the time of imaging, the combination of clinical and pathological findings gave sufficient

294   confidence in the diagnosis to allow treatment to be instigated; imaging was used to stage the cases and so

295   guide the intensity and duration of treatment. The evolution of changes over time in association with

296   treatment has not been described, and will be interesting to explore in the future. Finally, given the

297   retrospective nature of this study there are inconsistencies between cases with respect to factors such as

298   regions imaged and use of contrast medium. This leads to a bias in our results, and may underestimate

299   subclinical disease, particularly affecting the peripheral structures. As mentioned, the limited resolution of

300   smaller structures on VetMouseTrap™ scans contributes to this. However, the advantages of this technique

301   for disease screening, particularly in clinically compromised patients should not be ignored, and as faster

302   scanners become more commonplace many of the resolution difficulties will be eliminated.

303

304   **Conclusions**

305   As expected, the majority of CT changes noted in this study represent multisystemic disease,

306   typically with combinations of pulmonary infiltration, lymphadenomegaly and organomegaly. These

307   changes are strongly suggestive of infiltrative disease, differentials for which can include neoplasia (such as

308   lymphoma or mast cell disease), chronic inflammation/infectious processes (mycobacteriosis, feline

309   infectious peritonitis or systemic mycosis), hypereosinophilic syndrome and amyloidosis.[24] While no

310   abnormality has been recognised that is specific for mycobacteriosis, it is important that the potential for

311   mycobacterial infection is considered when these types of changes are identified in feline patients,

312   especially if they have non-specific clinical signs. In addition, when managing patients with a diagnosis of

313   mycobacteriosis, the potential for widespread clinical and sub-clinical abnormalities must be considered

314   and investigated in full.

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320   The authors do not have any potential conflict of interest to declare.

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326

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392

1   **Computed Tomographic Findings in Cats with Mycobacterial Infection**

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22   Keywords − feline, mycobacteriosis, computed tomography, infection, diagnosis

23

24   **Abstract**

25

26   **Objectives**

27   The objective of this study was to describe the imaging findings in computed tomography

28   (CT) associated with confirmed mycobacterial infection in cats.

29   **Methods**

30   CT images from 20 cats with confirmed mycobacterial disease were retrospectively

31   reviewed. Five cats underwent conscious full-body CT in a VetMouseTrap[TM] device. All

32   other cats had thoracic CT performed under general anaesthesia, with the addition of CT

33   investigation of the head/neck, abdomen and limbs in some cases.

34   **Results**

35   Mycobacterial infection was seen most frequently in adult (mean age 7.4 years; range

36   0.6-14 years) neutered male cats (11/20). The most common infections were

37   *Mycobacterium microti* (6/20) and *Mycobacterium bovis* (6/20). CT abnormalities were

38   most commonly seen in the thorax, consisting of bronchial (9/20), alveolar (8/20), ground

39   glass (6/20) or structured interstitial (15/20) lung patterns, which were often mixed.

40   Tracheobronchial, sternal and cranial mediastinal lymphadenomegaly were common

41   (16/20). Other abnormalities included abdominal (8/13) or peripheral (10/18)

42   lymphadenomegaly, hepatosplenomegaly (7/13), mixed osteolytic/osteoproliferative

43   skeletal lesions (7/20), and cutaneous or subcutaneous soft tissue masses/nodules (4/20).

44   **Conclusions and relevance**

45   CT of feline mycobacteriosis shows a wide range of abnormalities often involving

46   multiple organ systems and mimicking many other feline diseases. Mycobacteriosis

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47   should be considered in the differential diagnosis of thoracic, abdominal and skeletal

48   disorders in cats.

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Introduction

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53   Feline mycobacteriosis is a worldwide veterinary health concern, and although definitive data on

54 case numbers worldwide are lacking, mycobacterial infections in cats have been recognised with increasing

55 frequency in the UK, as well as being seen in many other countries. Mycobacterial disease in domestic cats

56 can result from infection by one of a number of species. The most commonly identified mycobacteria

57 include *Mycobacterium microti* and *Mycobacterium bovis*, which are primary pathogens and members of

58 the tuberculous complex group of mycobacteria.[1-3] Non-tuberculous mycobacterial species are less

59 commonly identified within clinically affected cats.[4]

60   Clinical presentation of mycobacterial infection in cats is variable, and is dependant primarily on

61 the species of mycobacteria involved and, importantly, the route of infection.[2,5-7] Historically, alimentary

62 lesions resulting from ingestion of milk from cows infected with *M. bovis* were most common; however

63 with overall reduction of tuberculosis in the national bovine herd since the early 1900's and widespread

64 pasteurisation of milk this is no longer the case.[8] Single or multiple cutaneous lesions with or without

65 lymph node involvement, and characteristically affecting the so-called 'fight and bite sites' (such as the

66 head and limbs), now represent the most common presentation of mycobacterial infection in cats: they

67 typically result from infection acquired from prey species.[3,9] Infection acquired through inhalation or

68 ingestion, resulting in respiratory or alimentary disease, is seen less frequently. The clinical presentation of

69 these forms of disease, and of disseminated disease resulting from haematogenous spread of infection, can

70 include non-specific signs such as weight loss, anorexia, coughing, anaemia, vomiting/diarrhoea,

71 hepatosplenomegaly, generalised lymphadenopathy and pyrexia.[7]

72   Definitive diagnosis of mycobacterial disease in cats can present significant problems, in part due

73 to difficulties in sample handling, and limitations in the available laboratory diagnostic techniques. As

74 such, mycobacterial infections are likely underdiagnosed within the domestic cat population. In addition to

75 significant morbidity resulting from primary infection, subclinical infection and recurrence of infection

76 following treatment are common.[7] Since significant and potentially fatal multisystemic disease can result

77 from infection with mycobacterial species, and since there are potential zoonotic risks associated with all

78 members of the tuberculosis complex,[7,10] identification and correct handling of potential cases is of the

79 upmost importance.

80   Previous publications detailing the diagnostic imaging findings in cats with confirmed

81   mycobacterial infection are limited to a single retrospective case series looking at survey radiographic

82   changes involving 33 cats,[11] and a number of isolated case reports describing the radiographic features of

83   feline mycobacteriosis.[12-14] Computed tomography is increasingly available to the veterinary community,

84   and it offers significant advantages over survey radiography by eliminating superimposition of anatomy,

85   having superior contrast resolution and being able to clarify intrathoracic lesions where radiographic

86   findings are negative or non-specific.[15,16] In addition, the decreased scan times which are achievable with

87   modern multi-detector scanners make CT a valuable tool in investigation of multisystemic disease in

88   clinically compromised patients. The CT features of mycobacterial disease in cats have not been described

89   previously. The aim of this paper was to review CT images from a large number of cats with confirmed

90   mycobacteriosis and to describe the range of abnormalities that can occur.

91

92   **Materials and Methods**

93   This study comprises a descriptive, retrospective case series. CT studies carried out between

94   August 2009 and January 2015, of cats with confirmed mycobacterial infection were submitted to one of

95   the authors (DGM). Inclusion criteria consisted of: (i) confirmation of mycobacterial infection and (ii) a CT

96   study of diagnostic quality. To confirm mycobacterial involvement, aspirated and/or biopsy samples of

97   affected tissue had been stained with Ziehl-Neelson (ZN) and found to have changes indicative of

98   mycobacteriosis.[1] Where possible, tissue culture,[17] interferon-gamma release assay, or PCR testing had

99   been used to identify which mycobacterial species was involved.[4,18,19]

100   Pseudonymised CT studies of the confirmed mycobacterial cases were examined without

101 knowledge of specific clinical information by a third year diagnostic imaging resident who was however

102 informed about the topic of the study (AM). To prevent bias by the assumption of disease, CT studies

103 covering the thorax and other body parts from an additional ten cats with confirmed non-mycobacterial

104 diseases were included and also pseudonymised. Images were evaluated using dedicated DICOM viewer

105 software (Osirix, Geneva, Switzerland, version 5.8.5-64bit) on a computer workstation (Apple Mac Pro,

106 Apple, USA) with a calibrated LCD flat screen monitor (Apple Cinemax Display, 30 inch, Apple, USA).

5

107   During the course of image evaluation, multi-planar reconstructions, maximum and minimum intensity

108   projections and variable windowing settings were used according to the preferences of the viewer.

109   CT studies were reviewed for the following diagnostic criteria: bronchial thickening; alveolar

110   pattern; ground glass opacity or structured interstitial lung change; evidence of pleural or pericardial

111   effusion, or pleural/mediastinal thickening; thoracic, abdominal or peripheral lymphadenomegaly, or lymph

112   node mineralisation; abdominal organomegaly, peritoneal effusion, other abdominal organ-associated

113   lesions; osteolysis or osteoproliferative changes; cutaneous/subcutaneous/oral/nasal lesions; or vascular and

114   dystrophic soft tissue calcification. The extent of any abnormality was characterised as focal, multifocal, or

115   diffuse. The degree of each change was graded as absent/normal, mild, moderate or severe.

116

117   **Results**

118   Twenty cats met the inclusion criteria. After all image interpretive data had been collected the

119   additional ten non-mycobacterial cat studies were identified and their data were excluded from further

120   analysis. The most common infections were *M. microti* and *M. bovis*, confirmed in 6/20 cases each. A non-

121   specified *M. tuberculosis* complex species was described in one case and in the remaining 7/20 cases the

122   species involved was not known. Eleven of the 20 cats were neutered males and 9/20 were neutered

123   females. The study group comprised 7/20 Domestic Short Hair, 4/20 Siamese, 2/20 Domestic Long Hair

124   and 1/20 of each of the following; Persian, Birman, Norwegian Forest Cat, Burmilla, British Short Hair,

125   Bengal and Maine Coon cats. The age of one cat was not known. For the remaining cats the mean age was

126   7.4 ± 3.8 years (range 0.6-14 years).

127   Five of the 20 cats underwent conscious full-body CT in a specific containing device

128   (VetMouseTrap™, University of Illinois at Urbana-Champaign, Urbana, IL).[20] The remaining 15 cats were

129   scanned under general anaesthesia, with images of the following body regions obtained: thorax only (2),

130   head/neck and thorax (3), thorax and abdomen (4), head/neck, thorax and abdomen (2), head/neck, thorax,

131   abdomen and single forelimb (2), head, thorax, bilateral tarsi/elbows (1), thorax and single hind limb (1).

132   Intravenous contrast medium (iopamidol or iohexol, 600-700mg I/kg) was administered to 12/20

133   cats, and post-contrast images of some or all body parts were obtained. Use of contrast medium depended

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134   on the findings in the pre-contrast images, the clinical condition of the cat, and the preferences of the

135   attending radiologist and primary clinician in each case.

136   Within the evaluated imaging studies, thoracic abnormalities were noted in 19/20 cases. Diffuse

137   bronchial thickening was present in 9/20 cats; being mild in eight cases and moderate in one. Eight cats

138   showed a focal alveolar pattern; mild in two cases, moderate in three cases and severe in three cases (Figure

139   1(a)). Diffuse or patchy ground glass opacity was noted in 6/20 cats; mild in three cases, moderate in two

140   cases and severe in one case. The most common pulmonary parenchymal change was a diffuse structured

141   interstitial pattern, which was present in 15/20 cats, being either nodular (7/15) or reticulonodular (8/15) in

142   nature; mild in six cases, moderate in five cases and severe in four cases (Figure 1(b,c)). Thoracic CT

143   images of 14/20 cats were considered to show a mixed pulmonary pattern, with a single pattern present in

144   4/20 cases. The appearance of the pulmonary parenchyma was normal in 2/20 cats, though one of these had

145   a thoracic lymphadenopathy despite normal lungs. Of the 20 cats, 16 had sternal, cranial mediastinal and/or

146   tracheobronchial lymphadenomegaly (Figure 2). Moderate lymphadenomegaly affecting the sternal or

147   tracheobronchial nodes was most common. One cat had moderate mineralisation of an enlarged cranial

148   mediastinal lymph node.

149   None of the cats had any evidence of pleural or pericardial effusion. One cat showed mild, diffuse

150   pleural thickening. One cat showed mild mineralisation of the aortic root. Two cats had regions of

151   cavitation within the lungs, associated in both cases with focal or multifocal nodular or alveolar changes

152   (Figure 3(a)). Three cats had scattered foci of mineralisation within the lungs, again associated with other

153   focal parenchymal changes (Figure 3(b)).

154   Thirteen of the 20 cats had imaging studies that included the abdomen. Abdominal

155   lymphadenomegaly was present in 8/13 cases and was typically generaliseddiffuse. The lymph nodes

156   affected could not always be individually identified, but included those of the celiac and cranial mesenteric

157   centres, which variably comprised the hepatic, splenic, gastric, pancreaticoduodenal, jejunal and colic

158   nodes. Lymphadenomegaly was mild in two cats, moderate in four cats and severe in two cats. In one cat

159   with a generalised moderate abdominal lymphadenomegaly, mild mineralisation of a mesenteric lymph

160   node was present (Figure 4(a)). Mild hepatomegaly was present in 3/13 cats and moderate hepatomegaly in

161   1/13. Mild splenomegaly was present in 6/13 cats and moderate splenomegaly in 1/13. Two cats with

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162   splenomegaly (one mild and one moderate) were also noted to show heterogeneity within the splenic

163   parenchyma following contrast medium administration. Additional abdominal organ changes were noted in

164   3/13 cats; one had a moderately enlarged pancreas, one had multiple nodules within both kidneys, and one

165   an irregular outline to the left kidney. Peritoneal effusion was not noted in any cat.

166   The appearance of the peripheral lymph nodes was assessed in 18/20 cats. The two cats not

167   included in this assessment had CT studies of the thorax only, without inclusion of any extra-thoracic

168   lymph node group. In 10/18 cases peripheral lymphadenomegaly was present, mild in 3/18, moderate in

169   2/18 and severe in 5/18. In 8/10 cats with lymphadenomegaly, the most significant enlargement was noted

170   in the mandibular and medial retropharyngeal nodes (Figure 4(b)); however, multifocal more diffuse

171   lymphadenomegaly, involving the superficial cervical (prescapular), axillary, inguinal and/or popliteal

172   nodes was variably present. In the other 2/10 cats, the head and neck were not imaged, but enlargement of

173   the superficial cervical and popliteal lymph nodes was noted respectively. Five of the eight cats in which

174   peripheral lymphadenomegaly was not noted underwent conscious CT in the VetMouseTrap™ device and

175   three underwent CT studies which did not include the head and neck.

176   Focal osteolytic lesions were present in 7/20 cats (although it was not possible to assess the entire

177   skeleton in 15 cats as they did not have full body CT examinations); changes were mild in four cases and

178   moderate in three cases. These lesions affected the nasal bridge in three cats and the limbs in the remaining

179   four, and were predominantly characterised by regions of cortical lysis (5/7) or erosive lesions at joint

180   surfaces (2/7) (Figure 5). An associated pathological long bone fracture was present in one case. In all but

181   one of these cases osteoproliferative changes, either periosteal reaction or periarticular osteophytosis, were

182   noted in the same location as the osteolytic change. The osteoproliferation was mild in three cases and

183   severe in three cases; however, the degree of proliferative change did not necessarily correlate with the

184   degree of lytic change in each case.

185   Cutaneous or subcutaneous lesions were only infrequently present within the studies evaluated.

186   Focal mass lesions over the nasal bridge were noted in 2/20 cats, graded moderate in one and severe in one.

187   One other cat had a small amount of fluid accumulation and soft tissue thickening in the dorsal nasal

188   chambers. Each of these lesions was adjacent to bony abnormalities. A focal, but extensive, mass lesion

189   was noted along the ventral head and neck of one cat. One cat was found to have multiple, widely

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190 distributed, subcutaneous nodules. Diffuse extra-thoracic dystrophic soft tissue mineralisation was not

191 noted in any cat.

192

193 **Discussion**

194 Mycobacteriosis in cats is known to be a highly variable disease, and should always be considered

195 as a possible differential diagnosis in cases which present with multisystemic signs. Mycobacterial disease

196 is likely under-recognised, primarily due to a lack of awareness of the full spectrum of changes which can

197 be associated with it.

198 Mycobacterial infection is most commonly seen in adult, neutered male cats consistent with the

199 results of our study.[9] Domestic Short Hair cats predominate in our study, but to a lesser degree than noted

200 in the previous radiographic case series (36% vs 87%).[11] The reason for this is unknown, but may reflect a

201 higher proportion of pedigree cats within a referral population, which are therefore more likely to undergo

202 advanced imaging.

203 CT abnormalities of the thorax were commonly noted, being present in all but one cat. However,

204 multisystemic abnormalities were also common, with changes affecting more than one anatomical region in

205 all but five cases. Of these five, three had abnormalities detected on clinical examination which were not

206 appreciable on the CT images. In cats, systemic mycobacterial infection is most commonly caused by *M.*

207 *bovis* or *M microti*,[3,9,21-24] and our results are consistent with this.

208 Previous reports of radiographic findings in cats with mycobacterial disease described a mild

209 predominance of a mixed lung pattern (ie, a combination of bronchial, alveolar and/or interstitial

210 changes),[1,9,11-13,22-24] but distinct alveolar, bronchial or interstitial patterns in isolation were also identified.[11]

211 Interestingly, where cases in our study displayed mixed lung patterns, bronchial thickening and ground

212 glass opacity were most commonly graded as mild, whereas alveolar pattern and structured interstitial

213 patterns were more likely to be moderate or severe. This is interesting for two reasons. Firstly, the mild

214 bronchial and unstructured interstitial patterns are of a degree that comparable changes may not be easily

215 visible radiographically, or may be attributed to expiratory or underexposed radiographs, or

216 superimposition of other structures. In a radiographic study it is therefore possible that only a more

217 significant overlying alveolar or nodular pattern may be recognised, leading to classification as a single

9

218   lung pattern. As superimposition effects are eliminated by CT, it becomes easier to identify these mild

219   changes in addition to the more marked ones. Secondly, a mild bronchial or unstructured interstitial pattern

220   may be indicative of concurrent conditions, such as low-grade allergic airway disease, rather than being

221   directly related to an active mycobacterial infection.[25,26] Differentiation of these may not be possible.

222   Within our study, the most commonly encountered single lung pattern was structured interstitial.

223   However, these cases could be further subdivided into cases displaying a nodular pattern, comprising

224   scattered rounded hyperattenuating foci, and a reticulonodular pattern, where rounded foci and linear or

225   sickle-shaped hyperattenuating structures overlie to give a more complex overall pattern. In humans, a

226   faint, diffuse reticulonodular pattern is considered characteristic of miliary tuberculosis.[27] While nodular

227   and reticulonodular patterns are distinguishable on good quality radiographs in cats, the distinction is only

228   rarely made in veterinary imaging. On CT however, the difference is more easily appreciable. The

229   diagnostic and prognostic significance of the variable patterns in feline patients is currently unknown, but

230   certainly warrants further investigation, as a structured interstitial pattern is a common finding in many

231   feline lung pathologies (eg, pulmonary fibrosis, metastatic neoplasia, eosinophilic bronchopneumopathy

232   and a wide range of infectious pneumonias).

233   It is interesting to note that within our study population, two cats were found to have cavitations

234   within their lungs. While this feature is relatively common in both humans and dogs with tuberculosis[28-30] it

235   was not noted in any case in the previous radiographic study of cats,[11] and the only paper which describes

236   cavitating tubercles in cats was published in 1949.[5] The lesions noted in the two cats in this study were

237   small (<1 cm) and were contained within regions of nodular or alveolar change. It is possible therefore that

238   they may not have been visible on radiographs, again highlighting the advantage of cross sectional imaging.

239   Alternatively, this may indeed reflect a rare occurrence in feline patients, which has occurred coincidentally

240   within our study population. In either case, it is an important characteristic to recognise, as cavitated lung

241   masses are occasionally identified in feline patients with lung neoplasia,[16,25] and the potential for

242   misdiagnosis exists in cats with mycobacteriosis which show this feature. In addition this should be

243   recognised because these cats likely pose an increased zoonotic risk compared with those showing the more

244   typical structured interstitial pattern as they may allow mycobacteria to gain access to the upper airways.

10

245   Thoracic lymphadenomegaly is a feature of numerous pulmonary and multisystemic conditions in

246   cats including, but not limited to, infiltrative and metastatic neoplasia, hypereosinophilic syndromes and

247   systemic mycosis/bacteriosis.[31] As expected thoracic lymphadenomegaly was commonly noted within our

248   study population, but in contrast to the findings of the previous radiographic paper, mild and moderate

249   enlargement predominated over severe.[11] This may reflect the difficulty in recognising minor changes on

250   radiographs. It is also worth noting that even given the superior contrast resolution of CT, with mild

251   lymphadenomegaly, particularly in the perihilar region; changes were more easily appreciated in post-

252   contrast studies when compared with pre-contrast. This suggests that there is value in performing post-

253   contrast scans in all cases (unless there is a clinical contraindication), which was not standard practice

254   within our study population.

255   Mineralisation of thoracic lymph nodes and pulmonary parenchyma can result from chronic

256   inflammation associated with mycobacterial infection;[9,13,32] it is also seen in cases of both primary and

257   metastatic pulmonary neoplasia, and chronic airways disease.[25] In either case, it is a finding which most

258   likely relates to the disease process that is present. In contrast, mild aortic root calcification, such as that

259   seen in one case (a seven year old cat) in our study is, in our experience, an occasional finding in middle

260   aged to older cats, and not necessarily related to clinical disease.

261   While peripheral and abdominal lymphadenomegaly were relatively common within the study

262   population, it is possible that the number of cases with mild or moderate lymphadenomegaly in the head

263   and neck was artificially low. This is because all cases recorded as having normal peripheral lymph nodes

264   on physical examination either did not undergo imaging of the head and neck, or were scanned conscious

265   within a VetMouseTrap[TM] device. The protocol for these scans involved a short scan time (in order to

266   minimise movement) resulting in a relatively large slice thickness and consequently a reduced longitudinal

267   resolution. This can compromise assessment of small structures so it is possible that mild or moderate

268   abnormalities of the head and neck, such as lymphadenomegaly, may have been overlooked. Other

269   abdominal changes such as hepatomegaly, splenomegaly, renal and pancreatic changes were noted

270   relatively infrequently and were mild or moderate in extent, consistent with previous reports.[9,11,12,33]

271   Two distinct manifestations of skeletal disease were noted within our population. The lesions

272   characterised by cortical lysis likely represent sites of primary bacterial inoculation and as such are

11

273 consistent in location with 'fight and bite' injuries; whereas periarticular abnormalities are consistent with

274 an infectious polyarthritis resulting from haematogenous dissemination of bacteria. It is interesting to note

275 that the appendicular skeletal lesions in this study were clinically evident, and affected regions were

276 intentionally included in the imaging studies. Clinically silent skeletal lesions may have been overlooked as

277 the limbs were excluded from the majority of studies. The only studies in which the limbs were included in

278 full were those performed using the VetMouseTrap™ device and it is possible that subtle or focal regions

279 of bone lysis or proliferation may not have been recognised due to the lower resolution of these studies.

280 Cutaneous lesions were noted infrequently in this study. While this may initially seem surprising,

281 given that cutaneous lesions represent a common presentation of mycobacteriosis,[3,9] it reflects the fact that

282 CT imaging is more likely to be employed in cases presenting with systemic disease, or used as a staging

283 tool in cats with clinically evident focal skin lesions without requirement for imaging of the lesions

284 themselves. The presence of intranasal changes in one cat is interesting, as these are indicative of a

285 mycobacterial rhinitis, a manifestation of respiratory mycobacteriosis which may not be commonly

286 recognised.

287 There are a number of limitations to this study. The most significant of these is that although

288 mycobacteriosis was confirmed in each case, histopathology on all involved tissues was not typically

289 performed; therefore, it is not possible to confirm that all changes seen were due to mycobacterial infection.

290 Due to the inherent difficulties in confirmation of mycobacterial infection, the time lapse between

291 acquisition of CT images and definitive confirmation of diagnosis was very variable; it extended to four

292 years and nine months in one case (though a lapse of one to four months was more typical). In all cases

293 however, at the time of imaging, the combination of clinical and pathological findings gave sufficient

294 confidence in the diagnosis to allow treatment to be instigated; imaging was used to stage the cases and so

295 guide the intensity and duration of treatment. The evolution of changes over time in association with

296 treatment has not been described, and will be interesting to explore in the future. Finally, given the

297 retrospective nature of this study there are inconsistencies between cases with respect to factors such as

298 regions imaged and use of contrast medium. This leads to a bias in our results, and may underestimate

299 subclinical disease, particularly affecting the peripheral structures. As mentioned, the limited resolution of

300 smaller structures on VetMouseTrap™ scans contributes to this. However, the advantages of this technique

12

301   for disease screening, particularly in clinically compromised patients should not be ignored, and as faster

302   scanners become more commonplace many of the resolution difficulties will be eliminated.

303

304   **Conclusions**

305   As expected, the majority of CT changes noted in this study represent multisystemic disease,

306   typically with combinations of pulmonary infiltration, lymphadenomegaly and organomegaly. These

307   changes are strongly suggestive of infiltrative disease, differentials for which can include neoplasia (such as

308   lymphoma or mast cell disease), chronic inflammation/infectious processes (mycobacteriosis, feline

309   infectious peritonitis or systemic mycosis), hypereosinophilic syndrome and amyloidosis.[24] While no

310   abnormality has been recognised that is specific for mycobacteriosis, it is important that the potential for

311   mycobacterial infection is considered when these types of changes are identified in feline patients,

312   especially if they have non-specific clinical signs. In addition, when managing patients with a diagnosis of

313   mycobacteriosis, the potential for widespread clinical and sub-clinical abnormalities must be considered

314   and investigated in full.

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320   The authors do not have any potential conflict of interest to declare.

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327   **References**

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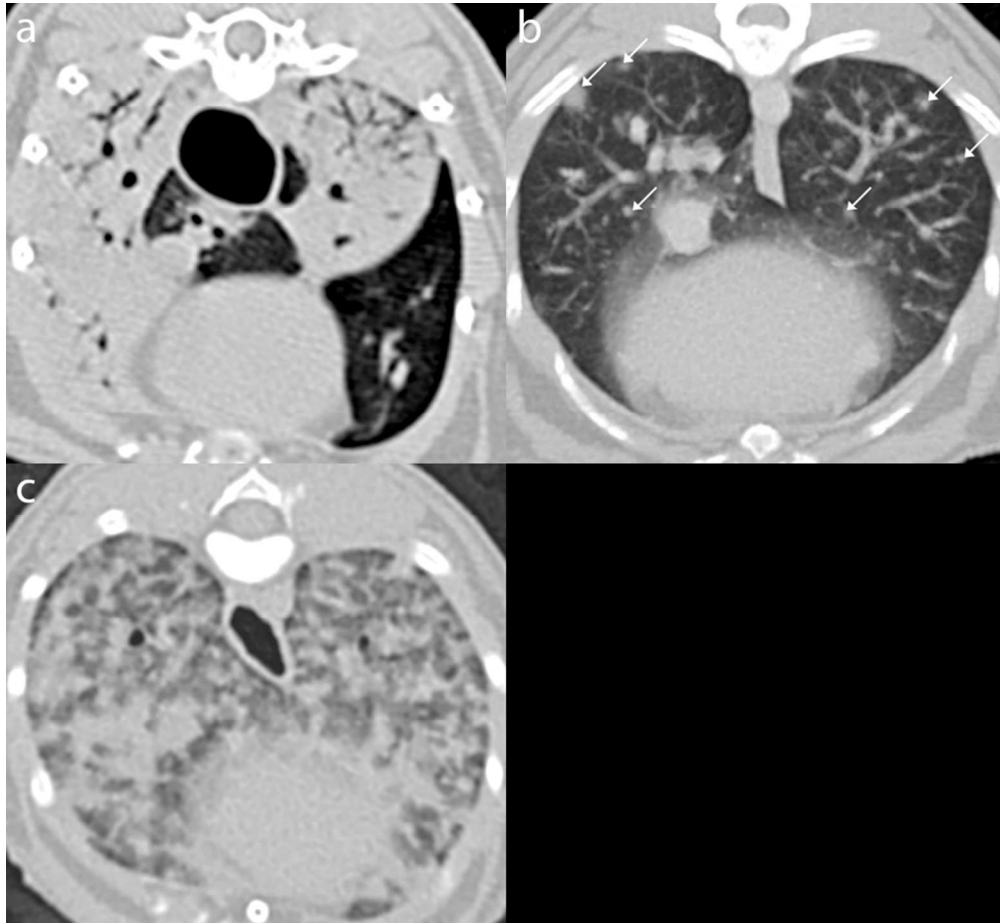391   Infection in a Persian cat. *J Vet Med* 2004; 51: 464-6.

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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
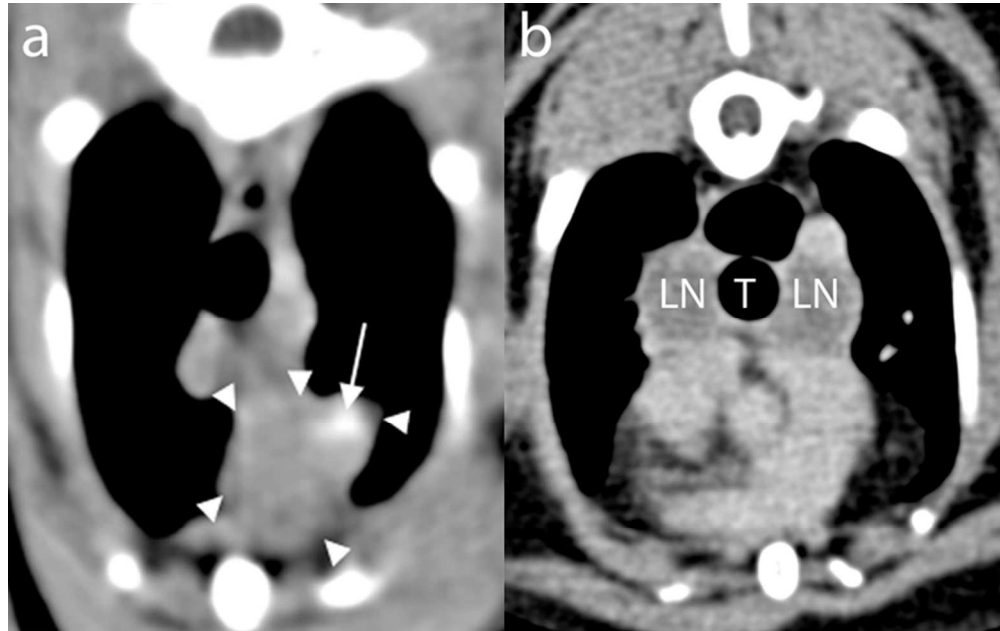91x84mm (300 x 300 DPI)

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
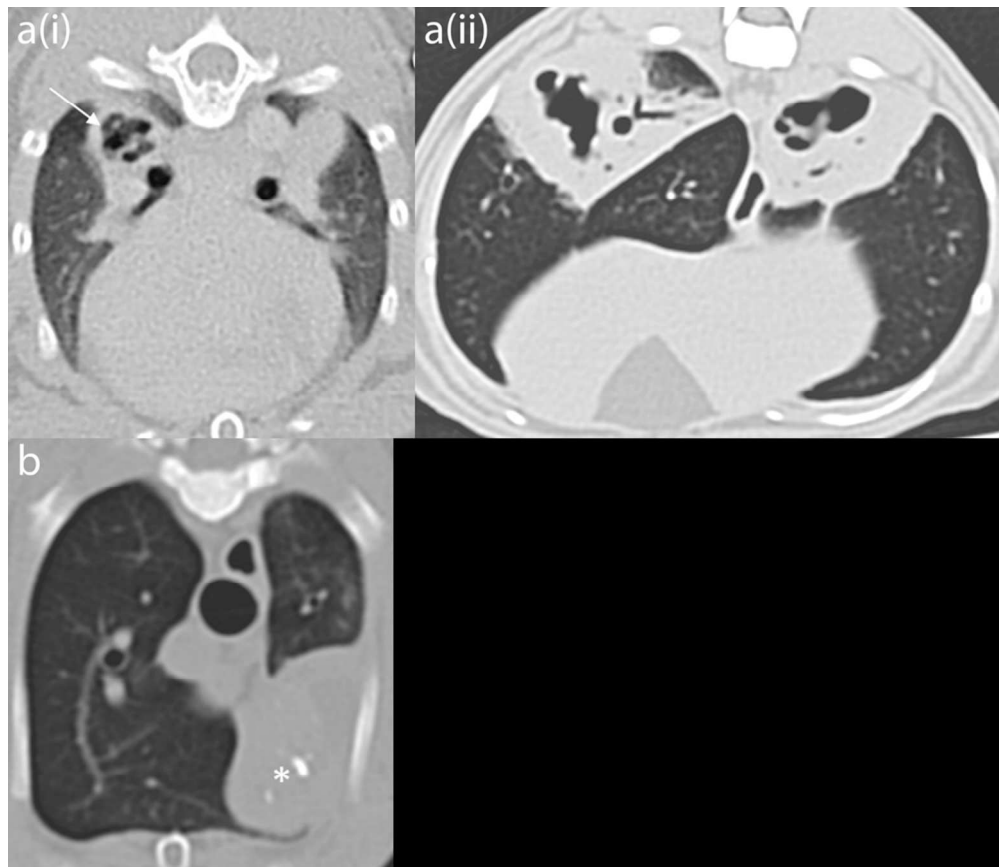134x84mm (300 x 300 DPI)

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 (*)
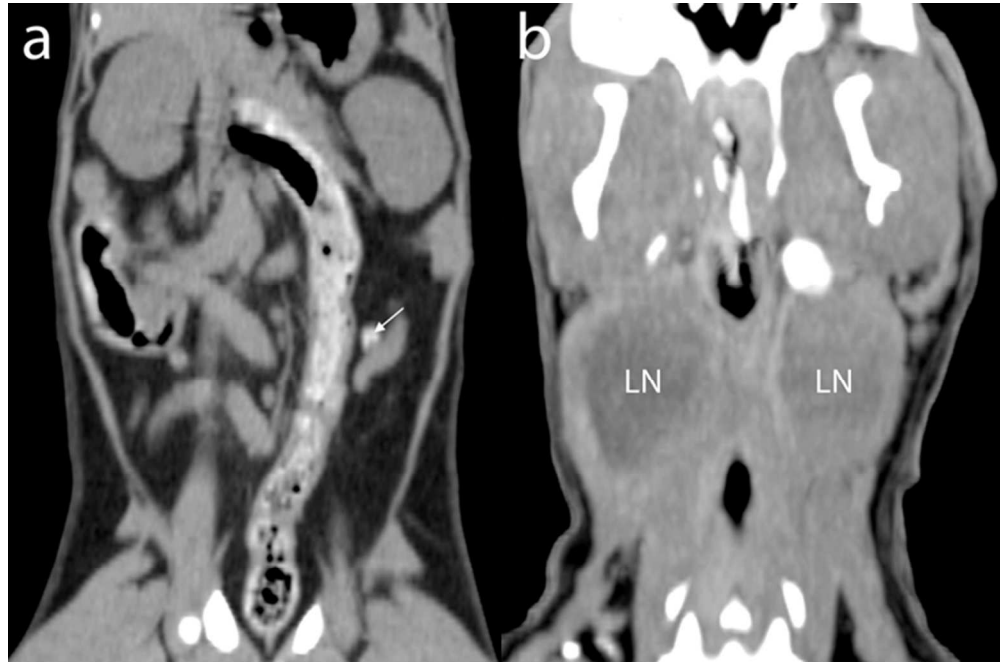98x84mm (300 x 300 DPI)

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)

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1   **Computed Tomographic Findings in Cats with Mycobacterial Infection**

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1

24   **Abstract**

25

26   **Objectives**

27   The objective of this study was to describe the imaging findings in computed tomography

28   (CT) associated with confirmed mycobacterial infection in cats.

29   **Methods**

30   CT images from 20 cats with confirmed mycobacterial disease were retrospectively

31   reviewed. Five cats underwent conscious full-body CT in a VetMouseTrap^{TM} device. All

32   other cats had thoracic CT performed under general anaesthesia, with the addition of CT

33   investigation of the head/neck, abdomen and limbs in some cases.

34   **Results**

35   Mycobacterial infection was seen most frequently in adult (mean age 7.4 years; range

36   0.6-14 years) neutered male cats (11/20). The most common infections were

37   *Mycobacterium microti* (6/20) and *Mycobacterium bovis* (6/20). CT abnormalities were

38   most commonly seen in the thorax, consisting of bronchial (9/20), alveolar (8/20), ground

39   glass (6/20) or structured interstitial (15/20) lung patterns, which were often mixed.

40   Tracheobronchial, sternal and cranial mediastinal lymphadenomegaly were common

41   (16/20). Other abnormalities included abdominal (8/13) or peripheral (10/18)

42   lymphadenomegaly, hepatosplenomegaly (7/13), mixed osteolytic/osteoproliferative

43   skeletal lesions (7/20), and cutaneous or subcutaneous soft tissue masses/nodules (4/20).

44   **Conclusions and relevance**

45   CT of feline mycobacteriosis shows a wide range of abnormalities often involving

46   multiple organ systems and mimicking many other feline diseases. Mycobacteriosis

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47　should be considered in the differential diagnosis of thoracic, abdominal and skeletal

48　disorders in cats.

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Introduction

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53   Feline mycobacteriosis is a worldwide veterinary health concern, and although definitive data on

54   case numbers worldwide are lacking, mycobacterial infections in cats have been recognised with increasing

55   frequency in the UK, as well as being seen in many other countries. Mycobacterial disease in domestic cats

56   can result from infection by one of a number of species. The most commonly identified mycobacteria

57   include *Mycobacterium microti* and *Mycobacterium bovis*, which are primary pathogens and members of

58   the tuberculous complex group of mycobacteria.[1-3] Non-tuberculous mycobacterial species are less

59   commonly identified within clinically affected cats.[4]

60   Clinical presentation of mycobacterial infection in cats is variable, and is dependant primarily on

61   the species of mycobacteria involved and, importantly, the route of infection.[2,5-7] Historically, alimentary

62   lesions resulting from ingestion of milk from cows infected with *M. bovis* were most common; however

63   with overall reduction of tuberculosis in the national bovine herd since the early 1900's and widespread

64   pasteurisation of milk this is no longer the case.[8] Single or multiple cutaneous lesions with or without

65   lymph node involvement, and characteristically affecting the so-called 'fight and bite sites' (such as the

66   head and limbs), now represent the most common presentation of mycobacterial infection in cats: they

67   typically result from infection acquired from prey species.[3,9] Infection acquired through inhalation or

68   ingestion, resulting in respiratory or alimentary disease, is seen less frequently. The clinical presentation of

69   these forms of disease, and of disseminated disease resulting from haematogenous spread of infection, can

70   include non-specific signs such as weight loss, anorexia, coughing, anaemia, vomiting/diarrhoea,

71   hepatosplenomegaly, generalised lymphadenopathy and pyrexia.[7]

72   Definitive diagnosis of mycobacterial disease in cats can present significant problems, in part due

73   to difficulties in sample handling, and limitations in the available laboratory diagnostic techniques. As

74   such, mycobacterial infections are likely underdiagnosed within the domestic cat population. In addition to

75   significant morbidity resulting from primary infection, subclinical infection and recurrence of infection

76   following treatment are common.[7] Since significant and potentially fatal multisystemic disease can result

77   from infection with mycobacterial species, and since there are potential zoonotic risks associated with all

78   members of the tuberculosis complex,[7,10] identification and correct handling of potential cases is of the

79   upmost importance.

4

80   Previous publications detailing the diagnostic imaging findings in cats with confirmed

81   mycobacterial infection are limited to a single retrospective case series looking at survey radiographic

82   changes involving 33 cats,[11] and a number of isolated case reports describing the radiographic features of

83   feline mycobacteriosis.[12-14] Computed tomography is increasingly available to the veterinary community,

84   and it offers significant advantages over survey radiography by eliminating superimposition of anatomy,

85   having superior contrast resolution and being able to clarify intrathoracic lesions where radiographic

86   findings are negative or non-specific.[15,16] In addition, the decreased scan times which are achievable with

87   modern multi-detector scanners make CT a valuable tool in investigation of multisystemic disease in

88   clinically compromised patients. The CT features of mycobacterial disease in cats have not been described

89   previously. The aim of this paper was to review CT images from a large number of cats with confirmed

90   mycobacteriosis and to describe the range of abnormalities that can occur.

91

92   **Materials and Methods**

93   This study comprises a descriptive, retrospective case series. CT studies carried out between

94   August 2009 and January 2015, of cats with confirmed mycobacterial infection were submitted to one of

95   the authors (DGM). Inclusion criteria consisted of: (i) confirmation of mycobacterial infection and (ii) a CT

96   study of diagnostic quality. To confirm mycobacterial involvement, aspirated and/or biopsy samples of

97   affected tissue had been stained with Ziehl-Neelson (ZN) and found to have changes indicative of

98   mycobacteriosis.[1] Where possible, tissue culture,[17] interferon-gamma release assay, or PCR testing had

99   been used to identify which mycobacterial species was involved.[4,18,19]

100   Pseudonymised CT studies of the confirmed mycobacterial cases were examined without

101   knowledge of specific clinical information by a third year diagnostic imaging resident who was however

102   informed about the topic of the study (AM). To prevent bias by the assumption of disease, CT studies

103   covering the thorax and other body parts from an additional ten cats with confirmed non-mycobacterial

104   diseases were included and also pseudonymised. Images were evaluated using dedicated DICOM viewer

105   software (Osirix, Geneva, Switzerland, version 5.8.5-64bit) on a computer workstation (Apple Mac Pro,

106   Apple, USA) with a calibrated LCD flat screen monitor (Apple Cinemax Display, 30 inch, Apple, USA).

5

107   During the course of image evaluation, multi-planar reconstructions, maximum and minimum intensity

108   projections and variable windowing settings were used according to the preferences of the viewer.

109   CT studies were reviewed for the following diagnostic criteria: bronchial thickening; alveolar

110   pattern; ground glass opacity or structured interstitial lung change; evidence of pleural or pericardial

111   effusion, or pleural/mediastinal thickening; thoracic, abdominal or peripheral lymphadenomegaly, or lymph

112   node mineralisation; abdominal organomegaly, peritoneal effusion, other abdominal organ-associated

113   lesions; osteolysis or osteoproliferative changes; cutaneous/subcutaneous/oral/nasal lesions; vascular and

114   dystrophic soft tissue calcification. The extent of any abnormality was characterised as focal, multifocal, or

115   diffuse. The degree of each change was graded as absent/normal, mild, moderate or severe.

116

117   **Results**

118   Twenty cats met the inclusion criteria. After all image interpretive data had been collected the

119   additional ten non-mycobacterial cat studies were identified and their data were excluded from further

120   analysis. The most common infections were *M. microti* and *M. bovis*, confirmed in 6/20 cases each. A non-

121   specified *M. tuberculosis* complex species was described in one case and in the remaining 7/20 cases the

122   species involved was not known. Eleven of the 20 cats were neutered males and 9/20 were neutered

123   females. The study group comprised 7/20 Domestic Short Hair, 4/20 Siamese, 2/20 Domestic Long Hair

124   and 1/20 of each of the following; Persian, Birman, Norwegian Forest Cat, Burmilla, British Short Hair,

125   Bengal and Maine Coon cats. The age of one cat was not known. For the remaining cats the mean age was

126   7.4 ± 3.8 years (range 0.6-14 years).

127   Five of the 20 cats underwent conscious full-body CT in a specific containing device

128   (VetMouseTrap™, University of Illinois at Urbana-Champaign, Urbana, IL).[20] The remaining 15 cats were

129   scanned under general anaesthesia, with images of the following body regions obtained: thorax only (2),

130   head/neck and thorax (3), thorax and abdomen (4), head/neck, thorax and abdomen (2), head/neck, thorax,

131   abdomen and single forelimb (2), head, thorax, bilateral tarsi/elbows (1), thorax and single hind limb (1).

132   Intravenous contrast medium (iopamidol or iohexol, 600-700mg I/kg) was administered to 12/20

133   cats, and post-contrast images of some or all body parts were obtained. Use of contrast medium depended

6

134   on the findings in the pre-contrast images, the clinical condition of the cat, and the preferences of the

135   attending radiologist and primary clinician in each case.

136   Within the evaluated imaging studies, thoracic abnormalities were noted in 19/20 cases. Diffuse

137   bronchial thickening was present in 9/20 cats; being mild in eight cases and moderate in one. Eight cats

138   showed a focal alveolar pattern; mild in two cases, moderate in three cases and severe in three cases (Figure

139   1(a)). Diffuse or patchy ground glass opacity was noted in 6/20 cats; mild in three cases, moderate in two

140   cases and severe in one case. The most common pulmonary parenchymal change was a diffuse structured

141   interstitial pattern, which was present in 15/20 cats, being either nodular (7/15) or reticulonodular (8/15) in

142   nature; mild in six cases, moderate in five cases and severe in four cases (Figure 1(b,c)). Thoracic CT

143   images of 14/20 cats were considered to show a mixed pulmonary pattern, with a single pattern present in

144   4/20 cases. The appearance of the pulmonary parenchyma was normal in 2/20 cats, though one of these had

145   a thoracic lymphadenopathy despite normal lungs. Of the 20 cats, 16 had sternal, cranial mediastinal and/or

146   tracheobronchial lymphadenomegaly (Figure 2). Moderate lymphadenomegaly affecting the sternal or

147   tracheobronchial nodes was most common. One cat had moderate mineralisation of an enlarged cranial

148   mediastinal lymph node.

149   None of the cats had any evidence of pleural or pericardial effusion. One cat showed mild, diffuse

150   pleural thickening. One cat showed mild mineralisation of the aortic root. Two cats had regions of

151   cavitation within the lungs, associated in both cases with focal or multifocal nodular or alveolar changes

152   (Figure 3(a)). Three cats had scattered foci of mineralisation within the lungs, again associated with other

153   focal parenchymal changes (Figure 3(b)).

154   Thirteen of the 20 cats had imaging studies that included the abdomen. Abdominal

155   lymphadenomegaly was present in 8/13 cases and was typically generalised. The lymph nodes affected

156   could not always be individually identified, but included those of the celiac and cranial mesenteric centres,

157   which variably comprised the hepatic, splenic, gastric, pancreaticoduodenal, jejunal and colic nodes.

158   Lymphadenomegaly was mild in two cats, moderate in four cats and severe in two cats. In one cat with a

159   generalised moderate abdominal lymphadenomegaly, mild mineralisation of a mesenteric lymph node was

160   present (Figure 4(a)). Mild hepatomegaly was present in 3/13 cats and moderate hepatomegaly in 1/13.

161   Mild splenomegaly was present in 6/13 cats and moderate splenomegaly in 1/13. Two cats with

7

162   splenomegaly (one mild and one moderate) were also noted to show heterogeneity within the splenic

163   parenchyma following contrast medium administration. Additional abdominal organ changes were noted in

164   3/13 cats; one had a moderately enlarged pancreas, one had multiple nodules within both kidneys, and one

165   an irregular outline to the left kidney. Peritoneal effusion was not noted in any cat.

166   The appearance of the peripheral lymph nodes was assessed in 18/20 cats. The two cats not

167   included in this assessment had CT studies of the thorax only, without inclusion of any extra-thoracic

168   lymph node group. In 10/18 cases peripheral lymphadenomegaly was present, mild in 3/18, moderate in

169   2/18 and severe in 5/18. In 8/10 cats with lymphadenomegaly, the most significant enlargement was noted

170   in the mandibular and medial retropharyngeal nodes (Figure 4(b)); however, multifocal

171   lymphadenomegaly, involving the superficial cervical (prescapular), axillary, inguinal and/or popliteal

172   nodes was variably present. In the other 2/10 cats, the head and neck were not imaged, but enlargement of

173   the superficial cervical and popliteal lymph nodes was noted respectively. Five of the eight cats in which

174   peripheral lymphadenomegaly was not noted underwent conscious CT in the VetMouseTrap™ device and

175   three underwent CT studies which did not include the head and neck.

176   Focal osteolytic lesions were present in 7/20 cats (although it was not possible to assess the entire

177   skeleton in 15 cats as they did not have full body CT examinations); changes were mild in four cases and

178   moderate in three cases. These lesions affected the nasal bridge in three cats and the limbs in the remaining

179   four, and were predominantly characterised by regions of cortical lysis (5/7) or erosive lesions at joint

180   surfaces (2/7) (Figure 5). An associated pathological long bone fracture was present in one case. In all but

181   one of these cases osteoproliferative changes, either periosteal reaction or periarticular osteophytosis, were

182   noted in the same location as the osteolytic change. The osteoproliferation was mild in three cases and

183   severe in three cases; however, the degree of proliferative change did not necessarily correlate with the

184   degree of lytic change in each case.

185   Cutaneous or subcutaneous lesions were only infrequently present within the studies evaluated.

186   Focal mass lesions over the nasal bridge were noted in 2/20 cats, graded moderate in one and severe in one.

187   One other cat had a small amount of fluid accumulation and soft tissue thickening in the dorsal nasal

188   chambers. Each of these lesions was adjacent to bony abnormalities. A focal, but extensive, mass lesion

189   was noted along the ventral head and neck of one cat. One cat was found to have multiple, widely

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190   distributed, subcutaneous nodules. Diffuse extra-thoracic dystrophic soft tissue mineralisation was not

191   noted in any cat.

192

193   **Discussion**

194   Mycobacteriosis in cats is known to be a highly variable disease, and should always be considered

195   as a possible differential diagnosis in cases which present with multisystemic signs. Mycobacterial disease

196   is likely under-recognised, primarily due to a lack of awareness of the full spectrum of changes which can

197   be associated with it.

198   Mycobacterial infection is most commonly seen in adult, neutered male cats consistent with the

199   results of our study.[9] Domestic Short Hair cats predominate in our study, but to a lesser degree than noted

200   in the previous radiographic case series (36% vs 87%).[11] The reason for this is unknown, but may reflect a

201   higher proportion of pedigree cats within a referral population, which are therefore more likely to undergo

202   advanced imaging.

203   CT abnormalities of the thorax were commonly noted, being present in all but one cat. However,

204   multisystemic abnormalities were also common, with changes affecting more than one anatomical region in

205   all but five cases. Of these five, three had abnormalities detected on clinical examination which were not

206   appreciable on the CT images. In cats, systemic mycobacterial infection is most commonly caused by *M.*

207   *bovis* or *M microti*,[3,9,21-24] and our results are consistent with this.

208   Previous reports of radiographic findings in cats with mycobacterial disease described a mild

209   predominance of a mixed lung pattern (ie, a combination of bronchial, alveolar and/or interstitial

210   changes),[1,9,11-13,22-24] but distinct alveolar, bronchial or interstitial patterns in isolation were also identified.[11]

211   Interestingly, where cases in our study displayed mixed lung patterns, bronchial thickening and ground

212   glass opacity were most commonly graded as mild, whereas alveolar pattern and structured interstitial

213   patterns were more likely to be moderate or severe. This is interesting for two reasons. Firstly, the mild

214   bronchial and unstructured interstitial patterns are of a degree that comparable changes may not be easily

215   visible radiographically, or may be attributed to expiratory or underexposed radiographs, or

216   superimposition of other structures. In a radiographic study it is therefore possible that only a more

217   significant overlying alveolar or nodular pattern may be recognised, leading to classification as a single

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218   lung pattern. As superimposition effects are eliminated by CT, it becomes easier to identify these mild

219   changes in addition to the more marked ones. Secondly, a mild bronchial or unstructured interstitial pattern

220   may be indicative of concurrent conditions, such as low-grade allergic airway disease, rather than being

221   directly related to an active mycobacterial infection.[25,26] Differentiation of these may not be possible.

222   Within our study, the most commonly encountered single lung pattern was structured interstitial.

223   However, these cases could be further subdivided into cases displaying a nodular pattern, comprising

224   scattered rounded hyperattenuating foci, and a reticulonodular pattern, where rounded foci and linear or

225   sickle-shaped hyperattenuating structures overlie to give a more complex overall pattern. In humans, a

226   faint, diffuse reticulonodular pattern is considered characteristic of miliary tuberculosis.[27] While nodular

227   and reticulonodular patterns are distinguishable on good quality radiographs in cats, the distinction is only

228   rarely made in veterinary imaging. On CT however, the difference is more easily appreciable. The

229   diagnostic and prognostic significance of the variable patterns in feline patients is currently unknown, but

230   certainly warrants further investigation, as a structured interstitial pattern is a common finding in many

231   feline lung pathologies (eg, pulmonary fibrosis, metastatic neoplasia, eosinophilic bronchopneumopathy

232   and a wide range of infectious pneumonias).

233   It is interesting to note that within our study population, two cats were found to have cavitations

234   within their lungs. While this feature is relatively common in both humans and dogs with tuberculosis[28-30] it

235   was not noted in any case in the previous radiographic study of cats,[11] and the only paper which describes

236   cavitating tubercles in cats was published in 1949.[5] The lesions noted in the two cats in this study were

237   small (<1 cm) and were contained within regions of nodular or alveolar change. It is possible therefore that

238   they may not have been visible on radiographs, again highlighting the advantage of cross sectional imaging.

239   Alternatively, this may indeed reflect a rare occurrence in feline patients, which has occurred coincidentally

240   within our study population. In either case, it is an important characteristic to recognise, as cavitated lung

241   masses are occasionally identified in feline patients with lung neoplasia,[16,25] and the potential for

242   misdiagnosis exists in cats with mycobacteriosis which show this feature. In addition this should be

243   recognised because these cats likely pose an increased zoonotic risk compared with those showing the more

244   typical structured interstitial pattern as they may allow mycobacteria to gain access to the upper airways.

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245   Thoracic lymphadenomegaly is a feature of numerous pulmonary and multisystemic conditions in

246   cats including, but not limited to, infiltrative and metastatic neoplasia, hypereosinophilic syndromes and

247   systemic mycosis/bacteriosis.[31] As expected thoracic lymphadenomegaly was commonly noted within our

248   study population, but in contrast to the findings of the previous radiographic paper, mild and moderate

249   enlargement predominated over severe.[11] This may reflect the difficulty in recognising minor changes on

250   radiographs. It is also worth noting that even given the superior contrast resolution of CT, with mild

251   lymphadenomegaly, particularly in the perihilar region; changes were more easily appreciated in post-

252   contrast studies when compared with pre-contrast. This suggests that there is value in performing post-

253   contrast scans in all cases (unless there is a clinical contraindication), which was not standard practice

254   within our study population.

255   Mineralisation of thoracic lymph nodes and pulmonary parenchyma can result from chronic

256   inflammation associated with mycobacterial infection;[9,13,32] it is also seen in cases of both primary and

257   metastatic pulmonary neoplasia, and chronic airways disease.[25] In either case, it is a finding which most

258   likely relates to the disease process that is present. In contrast, mild aortic root calcification, such as that

259   seen in one case (a seven year old cat) in our study is, in our experience, an occasional finding in middle

260   aged to older cats, and not necessarily related to clinical disease.

261   While peripheral and abdominal lymphadenomegaly were relatively common within the study

262   population, it is possible that the number of cases with mild or moderate lymphadenomegaly in the head

263   and neck was artificially low. This is because all cases recorded as having normal peripheral lymph nodes

264   on physical examination either did not undergo imaging of the head and neck, or were scanned conscious

265   within a VetMouseTrap[TM] device. The protocol for these scans involved a short scan time (in order to

266   minimise movement) resulting in a relatively large slice thickness and consequently a reduced longitudinal

267   resolution. This can compromise assessment of small structures so it is possible that mild or moderate

268   abnormalities of the head and neck, such as lymphadenomegaly, may have been overlooked. Other

269   abdominal changes such as hepatomegaly, splenomegaly, renal and pancreatic changes were noted

270   relatively infrequently and were mild or moderate in extent, consistent with previous reports.[9,11,12,33]

271   Two distinct manifestations of skeletal disease were noted within our population. The lesions

272   characterised by cortical lysis likely represent sites of primary bacterial inoculation and as such are

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273 consistent in location with 'fight and bite' injuries; whereas periarticular abnormalities are consistent with

274 an infectious polyarthritis resulting from haematogenous dissemination of bacteria. It is interesting to note

275 that the appendicular skeletal lesions in this study were clinically evident, and affected regions were

276 intentionally included in the imaging studies. Clinically silent skeletal lesions may have been overlooked as

277 the limbs were excluded from the majority of studies. The only studies in which the limbs were included in

278 full were those performed using the VetMouseTrap™ device and it is possible that subtle or focal regions

279 of bone lysis or proliferation may not have been recognised due to the lower resolution of these studies.

280 Cutaneous lesions were noted infrequently in this study. While this may initially seem surprising,

281 given that cutaneous lesions represent a common presentation of mycobacteriosis,[3,9] it reflects the fact that

282 CT imaging is more likely to be employed in cases presenting with systemic disease, or used as a staging

283 tool in cats with clinically evident focal skin lesions without requirement for imaging of the lesions

284 themselves. The presence of intranasal changes in one cat is interesting, as these are indicative of a

285 mycobacterial rhinitis, a manifestation of respiratory mycobacteriosis which may not be commonly

286 recognised.

287 There are a number of limitations to this study. The most significant of these is that although

288 mycobacteriosis was confirmed in each case, histopathology on all involved tissues was not typically

289 performed; therefore, it is not possible to confirm that all changes seen were due to mycobacterial infection.

290 Due to the inherent difficulties in confirmation of mycobacterial infection, the time lapse between

291 acquisition of CT images and definitive confirmation of diagnosis was very variable; it extended to four

292 years and nine months in one case (though a lapse of one to four months was more typical). In all cases

293 however, at the time of imaging, the combination of clinical and pathological findings gave sufficient

294 confidence in the diagnosis to allow treatment to be instigated; imaging was used to stage the cases and so

295 guide the intensity and duration of treatment. The evolution of changes over time in association with

296 treatment has not been described, and will be interesting to explore in the future. Finally, given the

297 retrospective nature of this study there are inconsistencies between cases with respect to factors such as

298 regions imaged and use of contrast medium. This leads to a bias in our results, and may underestimate

299 subclinical disease, particularly affecting the peripheral structures. As mentioned, the limited resolution of

300 smaller structures on VetMouseTrap™ scans contributes to this. However, the advantages of this technique

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301   for disease screening, particularly in clinically compromised patients should not be ignored, and as faster

302   scanners become more commonplace many of the resolution difficulties will be eliminated.

303

304   **Conclusions**

305   As expected, the majority of CT changes noted in this study represent multisystemic disease,

306   typically with combinations of pulmonary infiltration, lymphadenomegaly and organomegaly. These

307   changes are strongly suggestive of infiltrative disease, differentials for which can include neoplasia (such as

308   lymphoma or mast cell disease), chronic inflammation/infectious processes (mycobacteriosis, feline

309   infectious peritonitis or systemic mycosis), hypereosinophilic syndrome and amyloidosis.[24] While no

310   abnormality has been recognised that is specific for mycobacteriosis, it is important that the potential for

311   mycobacterial infection is considered when these types of changes are identified in feline patients,

312   especially if they have non-specific clinical signs. In addition, when managing patients with a diagnosis of

313   mycobacteriosis, the potential for widespread clinical and sub-clinical abnormalities must be considered

314   and investigated in full.

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320   The authors do not have any potential conflict of interest to declare.

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393   **Figure 1. CT appearance of lung parenchyma in three cats with mycobacteriosis, at the level of the**

394   **accessory lung lobe. (a) Alveolar pattern affecting multiple lung lobes. (b) Diffuse structured**

395   **interstitial pattern comprising multiple relatively well defined nodules (arrows). (c) Diffuse**

396   **structured interstitial pattern comprising mixed nodular and linear structures, characteristic of a**

397   **reticulonodular pattern**

398

399   **Figure 2. Thoracic lymphadenopathy in two cats with mycobacteriosis. (a) Transverse thoracic CT**

400   **image at the level of the third sternebra showing an enlarged cranial mediastinal lymph node**

401   **(arrowheads) containing a focus of mineralisation (arrow). (b) Post-contrast transverse CT image at**

402   **the level of the cardiac base showing bilaterally enlarged tracheobronchial lymph nodes (LN)**

403   **surrounding the trachea (T). The use of contrast medium allows differentiation from the cardiac and**

404   **vascular structures**

405

406   **Figure 3. Less common thoracic abnormalities in three cats with mycobacteriosis. (a(i)) Transverse**

407   **thoracic CT image at the level of the caudal mainstem bronchi showing a partially cavitated nodule**

408   **(arrow). (a(ii)) Transverse thoracic CT image at the level of the accessory lung lobe showing more**

409   **extensive parenchymal cavitation (b) Transverse thoracic CT image at the level of the third thoracic**

410   **vertebra showing a region of alveolar pattern containing mineralised foci (*)**

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16

412   **Figure 4. Extrathoracic lymphadenomegaly in two cats with mycobacteriosis. (a) Dorsal plane CT**

413   **reconstruction of the abdomen at the level of the descending colon in a cat with a partially**

414   **mineralised colic lymph node (arrow). (b) Dorsal plane CT reconstruction of the ventral neck in a cat**

415   **with marked bilateral medial retropharyngeal lymphadenomegaly (LN)**

416

417   **Figure 5. Bony lesions in four cats with mycobacteriosis. (a) Transverse CT image at the level of the**

418   **canine teeth, demonstrating focal lysis (arrowhead) and moderate, irregular periosteal reaction**

419   **(arrow). These is a soft tissue mass lesion associated with the bony change (*). (b) Transverse CT**

420   **image at the level of the proximal radius and ulna which shows focal cortical lysis of the ulna**

421   **(arrows) and marked smooth periosteal reaction. The adjacent radius is normal. (c) Sagittal plane**

422   **CT reconstruction of the radius and ulna in a cat with a pathological fracture secondary to a**

423   **tuberculous lesion. Lytic foci are visible in the distal radius (arrows), and there is a moderate smooth**

424   **periosteal reaction (arrowhead). The adjacent ulna is normal. (d) Transverse CT image at the level of**

425   **the humeral condyle showing marked periarticular new bone formation in a cat with a mycobacterial**

426   **polyarthritis**

17