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Comparison of the chest computed tomography findings between patients with pulmonary tuberculosis and those with Mycobacterium avium complex lung disease

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6 **tuberculosis and those with *Mycobacterium avium* complex lung disease**

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31

32

33 **Abstract**

34 **Background:** Since the computed tomography (CT) findings of nontuberculous mycobacterial
35 lung disease are similar to those of pulmonary tuberculosis (PTB), we often have difficulty
36 differentiating the two. In this study, we compared the differences in chest CT findings and their
37 locations between cases of PTB and *Mycobacterium avium* complex lung disease (MACLD).

38 **Methods:** The subjects were 100 MACLD patients and 42 PTB patients treated at our hospital
39 from May 2005 to August 2015. The CT findings were retrospectively evaluated. **Results:** PTB
40 more frequently showed lung shadows with calcification inside the lesion, calcification of the
41 mediastinal/hilar lymph node, and pleural effusion on CT than MACLD, while extensive
42 bronchiectasis and granular/large shadows connected to bronchiectasis were more frequently
43 observed with MACLD than PTB. For cavitary lesions, the thinnest part of the cavity wall with
44 MACLD was thinner than that with PTB. Granular shadows, large shadows, and bronchiectasis
45 were typically distributed to the right upper lobe and left upper division in PTB cases vs. the right
46 intermediate lobe and left lingula in MACLD. **Conclusions:** Chest CT findings would therefore
47 be useful for distinguishing PTB and MACLD when typical findings are observed.

48

49 **Keywords:** CT findings, tuberculosis, *Mycobacterium avium* complex, differential diagnosis

50

51 **Abbreviations:** CT, computed tomography; PTB, pulmonary tuberculosis; MAC,

52 *Mycobacterium avium* complex; MACLD, *Mycobacterium avium* complex lung disease; NTMLD,

53 nontuberculous mycobacterial lung disease; RUL, right upper lobe; LUD, left upper division; S,

54 Segment; RIL, right intermediate lobe; LL, left lingula; RS6, right segment 6; LS6, left segment

55 6; RBS, right basal segmental of the lung; LBS, left basal segmental of the lung; BE,

56 bronchiectasis; HRCT, high-resolution computed tomography.

57

58

59 **1. Introduction**

60 The number of pulmonary nontuberculous mycobacterial lung disease (NTMLD) cases has
61 reportedly increased worldwide in recent years [1]. In Japan, the estimated morbidity rate of
62 NTMLD was 5.7 in a population of 100,000 in 2007, increasing to 14.7 in 2014 [2], and
63 *Mycobacterium avium* complex lung disease (MACLD) caused by infection with *Mycobacterium*
64 *avium* or *Mycobacterium intracellulare* accounts for about 85% of cases of NTMLD [3].
65 Respiratory physicians often encounter MACLD during routine practice, e.g., during medical
66 checkups or cancer screening tests.

67 The morbidity rate of tuberculosis in 2017 was 13.3 per 100,000 persons in Japan [4].
68 While a decreasing trend has been noted, the morbidity rate is still higher in Japan than in other
69 developed countries. When managing pulmonary tuberculosis (PTB) cases, it is necessary to
70 consider airborne infection control; however, this is not necessary in NTMLD cases. Therefore,
71 to first determine the appropriate infection control strategy and therapy, careful evaluation of chest
72 computed tomography (CT) image findings is very important. However, since there are many
73 similarities in CT findings between NTMLD and PTB, clinicians often face difficulty
74 differentiating the two. In Japan, the majority of pulmonary NTMLD cases are MACLD cases;
75 therefore, differentiation of MACLD and PTB is frequently required. Although several reports
76 from Asian countries have compared CT images of NTMLD and PTB [5-7], the proportions of

77 nontuberculous mycobacterium species differ (i.e., the proportion of *M. abscessus* is high).

78 Although a few papers have compared the chest CT findings in MACLD and PTB [8, 9], over

79 two decades have passed since the most recent publication.

80 Working under the hypothesis that new findings might have become available in recent

81 years and/or that differences in CT findings between MACLD and PTB might now be detectable,

82 we analyzed and compared the differences in chest CT findings and their locations between adult

83 cases of MACLD and PTB. We attempted to evaluate the CT findings as simply and objectively

84 as possible.

85

86

87 **2. Patients and methods**

88 *2.1. Subjects and diagnosis criteria*

89 This retrospective study included subjects meeting the diagnostic criteria of MACLD or
90 PTB from May 2005 to August 2015 in Shimane University Hospital. Patients with MACLD who
91 met all of the following criteria were included: (1) chest CT images consistent with pulmonary
92 MACLD; (2) other diseases were excluded; (3) sputum culture positive in two or more different
93 specimens, or culture positive from one or more bronchial lavage fluid specimens. All extracted
94 cases with MACLD met the NTMLD diagnostic criteria of the Japanese Respiratory
95 Society/Japanese Society for Tuberculosis [10]. Patients with PTB all showed *M. tuberculosis* in
96 at least one sputum sample. We excluded patients who did not undergo chest CT at our hospital,
97 had a history of PTB or MACLD treatment, and had a clear association with active lung diseases,
98 such as lung cancer and or bacterial pneumonia.

99 This study was approved on February 28, 2014 by the Shimane University Institutional
100 Committee on Ethics (approval number is 1507), and the requirement for written informed
101 consent was waived because of the retrospective design.

102

103 *2.2. CT imaging conditions*

104 We evaluated the CT images obtained on the day of or the closest date to the diagnosis of

105 MACLD or PTB. CT was performed using any of the following devices: TSX-101A, TSX-
106 301A/2, or TSX-301X (Toshiba Medical Systems, Tokyo, Japan); or Brilliance 40 CT or
107 Brilliance 64 CT (Philips Medical Systems, Amsterdam, Netherlands). The imaging conditions
108 were as follows: lung field condition = window level 600, window width 1600; mediastinal
109 condition = window level +30, window width 300. The slice thickness at our hospital was
110 basically set at 5 mm, with a slice thickness of ≤ 2 mm regarded as high-resolution CT (HRCT).

111

112 2.3. Evaluation of imaging findings

113 Abnormal findings in the lung field were classified as follows: (A) granular shadow,
114 shadow with a major axis of ≤ 1 cm; (B) nodular shadow, oval lesion with a clearly distinguishable
115 boundary and a major axis of >1 cm; (C) large shadow, shadow with a major axis of >1 cm,
116 including adhesive shadow, invasive shadow, and atelectasis; (D) bronchiectasis, when the
117 bronchial lumen is more dilated than the central side, the bronchial lumen is clearly thicker than
118 the diameter of the pulmonary artery running in parallel, or the lumen of bronchus can be clearly
119 observed within 1 cm of the pleura; (E) cavitory lesions; (F) tree-in-bud appearance; (G) granular
120 shadow connected to bronchiectasis; and (H) large shadow connected to bronchiectasis (Figure
121 1).

122 We evaluated the findings at each of eight sites: right upper lobe (RUL); left upper division

123 (LUD), Segment (S) 1+2 and S3; right intermediate lobe (RIL); left lingula (LL), S4 and S5; right
124 S6 (RS6); left S6 (LS6); right basal segmental of the lung (RBS), S7 to S10; and left basal
125 segmental of the lung (LBS), S8 to S10. Cavitory lesions were additionally evaluated in terms of
126 the number of cavities, maximum diameter of the cavity, thickest part of the cavity wall, and
127 length of the thinnest part.

128 We also evaluated the calcification of the mediastinal/hilar lymph node, pulmonary
129 emphysema, honeycomb lung, pneumoconiosis, pleural effusion, and calcification inside the
130 shadow within the lung.

131 These findings were evaluated based on discussions between two pulmonologists and one
132 radiologist who were blinded to the patients' clinical information.

133

134 *2.4. Statistical analyses*

135 Computer software programs were used for the statistical analyses (IBM SPSS statistics
136 version 20; IBM, New York, United States of America). For comparisons between groups, a *t*-test
137 was used for the continuous data and the chi-squared test was used for descriptive data. A p-value
138 ≤ 0.05 was considered significant.

139

140 **3. Results**

141 *3.1. Patient background and characteristics*

142 The study population consisted of 100 MACLD patients and 42 PTB patients. Among the
143 100 patients with MACLD, *M. avium* was detected in 47 cases, *M. intracellulare* in 40 cases, and
144 both in 13 cases. Among the subjects with MACLD, chest CT showed the so-called nodular-
145 bronchiectasis type lesions in 67 cases and cavitary-type lesions in 13 patients. However, in 20
146 cases, it was difficult to clearly distinguish due to the coexistence of both lesions. Among the 42
147 patients with PTB, 5 cases were associated with miliary tuberculosis, and 6 were associated with
148 tuberculous pleurisy. HRCT was performed in 99 cases (99%) of MACLD and 38 cases (90.5%)
149 of PTB.

150 The subjects with MACLD included 29 males and 71 females, with the mean age of 71.5
151 \pm 11.0 years, whereas those with PTB included 30 males and 12 females, with the mean age of
152 73.9 ± 16.8 years. The proportion of males was lower in the MACLD cases and greater in the
153 PTB cases ($p < 0.001$). The immunocompromised patients (those with poorly controlled diabetes,
154 advanced renal impairment, liver failure, lymphocytopenia [$<1,000/\mu\text{L}$], taking
155 immunosuppressive drugs, or receiving anti-cancer drug treatment) included 38 with MACLD
156 and 28 with PTB, indicating a significantly higher incidence of PTB in this population ($p = 0.002$)
157 (Table 1). All subjects were Japanese citizens living in Shimane Prefecture. There were no cases
158 complicated with human immunodeficiency virus infection or cystic fibrosis in this study.

159

160 *3.2. Characteristics of granular shadow, large shadow, bronchiectasis, and cavities*

161 Granular shadows were observed frequently with both diseases (MACLD 95% vs. PTB
162 100%, $p = 0.168$), while nodular shadows were relatively infrequent (MACLD 7% vs. PTB 16.7%,
163 $p = 0.076$). The frequency of large shadows and cavitary lesions was similar between the two
164 groups (MACLD 67% vs. PTB 76.2%, $p = 0.277$; MACLD 36% vs. PTB 26.2%, $p = 0.257$;
165 respectively). Bronchiectasis was significantly more frequently observed with MACLD than with
166 PTB (MACLD 93% vs. PTB 42.9%, $p < 0.001$) (Table 2). Among the patients showing
167 bronchiectasis, when the left upper lobe was counted by dividing it into LUD and LL, the average
168 number of pulmonary lobes showing bronchiectasis was significantly larger in patients with
169 MACLD (3.87 ± 1.66) than in those with PTB (2.11 ± 1.53) ($p < 0.001$) (Table 3).

170 The frequency of granular shadow disseminated in the airway and connected to
171 bronchiectasis was 81% in MACLD cases vs. 26.2% in PTB cases ($p < 0.001$), while that of a
172 large shadow connected to bronchiectasis was 56% in MACLD cases vs. 7.1% in PTB cases ($p <$
173 0.001), with both indicating a significantly higher frequency with MACLD than with PTB. There
174 were no significant differences between the two groups regarding the presence of tree-in-bud
175 signs (MACLD 68% vs. PTB 64.3%, $p = 0.668$). Lesions with calcification inside the lung shadow
176 were significantly more frequently observed with PTB than with MACLD (MACLD 30% vs.

177 PTB 61.9%, $p < 0.001$) (Table 2).

178 There were no significant differences in the average number of cavities (MACLD $3.06 \pm$
179 3.26 vs. PTB 2.73 ± 1.49 ; $p = 0.749$) or the maximum diameter of the cavity (29.6 ± 21.3 mm vs.
180 34.9 ± 16.7 mm; $p = 0.457$). The thickest part of the cavity wall tended to be thicker in patients with
181 PTB (4.89 ± 3.07 mm vs. 7.91 ± 4.95 mm; $p = 0.079$), while the thinnest part was significantly
182 thinner in patients with MACLD (2.36 ± 1.40 mm vs. 3.64 ± 2.46 mm; $p = 0.034$) (Table 3).

183

184 *3.3. Distribution of granular shadow, large shadow, bronchiectasis, and cavities*

185 The frequency at which a granular shadow was observed in the RUL/LUD was
186 significantly higher in patients with PTB (MACLD 78% vs. PTB 92.9%, $p = 0.034$), while that
187 in the RIL/LL was significantly higher in patients with MACLD (MACLD 84% vs. PTB 61.9%,
188 $p = 0.004$) (Table 4). Similarly, the frequency at which a large shadow was observed in the
189 RUL/LUD was significantly higher in patients with PTB (MACLD 30% vs. PTB 64.3%, $p <$
190 0.001), while that in the RIL/LL tended to be higher in patients with MACLD (MACLD 51% vs.
191 PTB 33.3%, $p = 0.054$) (Table 5).

192 The frequency at which bronchiectasis was observed was higher in patients with MACLD
193 overall, and especially in the RIL/LL (MACLD 82% vs. PTB 14.3%, $p < 0.001$). The presence of
194 bronchiectasis in both the RIL and LL was observed with a moderate frequency in MACLD

195 patients, but was only rarely observed in PTB patients (MACLD 58% vs. PTB 2.4%, $p < 0.001$)
196 (Table 6). Bronchiectasis in PTB patients tended to present in the RUL/LUD. No cavitary lesions
197 were observed in the RIL/LL among PTB cases (MACLD 14% vs. PTB 0%, $p = 0.038$) (Table 7).

198

199 *3.4. Other CT findings*

200 The frequencies of calcification of the mediastinal/hilar lymph node, pleural effusion, and
201 calcification inside the lung shadow were significantly higher with PTB than with MACLD
202 (MACLD 12% vs. PTB 42.9%, $p < 0.001$; MACLD 4% vs. PTB 38.1%, $p < 0.001$; and MACLD
203 30% vs. PTB 61.9%, $p < 0.001$; respectively). The frequencies of emphysema, honeycomb lung,
204 and pneumoconiosis were similar between the two groups (MACLD 19% vs. PTB 31%, $P =$
205 0.120 ; MACLD 7% vs. PTB 4.8%, $p = 0.471$; MACLD 0% vs. PTB 4.8%, $p = 0.086$; respectively)
206 (Table 2).

207 We compared the frequency of CT findings between normal-immune patients and
208 immunodeficient, respectively patients with MACLD and those with PTB. The results showed no
209 obvious difference in the frequency of shadows between normal-immune and immunodeficient
210 MACLD patients. However, among PTB patients, the frequency of tree-in-bud signs was higher
211 in normal-immune patients (85.7% of 14 normal-immune patients vs. 53.6% of 28
212 immunodeficient, $p = 0.040$), and the frequency of pleural effusion was higher in

213 immunodeficient patients (7.1% normal-immune patients vs. 53.6% immunodeficient, $p = 0.003$).

214

215 **4. Discussion**

216 Bronchiectasis is an important lesion that is frequently observed in NTMLD cases [11] and
217 is thought to be caused by chronic inflammation mainly in the bronchioles and bronchus [12-14].
218 However, bronchiectasis is also commonly observed in PTB cases [15], where it is thought to be
219 caused by inflammation in the bronchioles, bronchial obstruction, and granulomatous lesions
220 occupying the airway in cases of active infection [16,17]. Furthermore, after healing from PTB,
221 the loss of lung volume causes traction bronchiectasis [18].

222 Previous comparative studies have shown that bronchiectasis is more frequently observed
223 and tends to exist in multiple pulmonary lobes in the CT findings of MACLD in comparison to
224 the findings of PTB [8, 9]. Similarly, in our study, MACLD cases showed more extensive
225 bronchodilation than PTB cases and cases showing bronchiectasis in both the RIL and LL were
226 rarely observed among PTB patients. The CT findings in MACLD have been reported to indicate
227 more centrilobular granular shadows around the areas of bronchodilation [19], with a frequency
228 that is significantly higher than that in PTB patients [9]. In the present study, we evaluated the
229 granular shadows connected to bronchiectasis, and showed that such CT findings were also more
230 frequently observed in MACLD cases than in PTB cases.

231 Findings such as adhesive shadows, consolidation, and atelectasis are commonly
232 observed in the chest CT images of MACLD patients. They are thought to be created due to the

233 enhancement of centrilobular granular shadows over time. In routine practice, these shadows
234 (adhesive shadows, consolidation, and atelectasis), like granular shadows, are often found to be
235 continuous with bronchiectasis, which we suspect to be a characteristic of MACLD. However, no
236 previous reports have compared MACLD to PTB by evaluating the connection of these shadows
237 to bronchiectasis as CT findings. A possible reason for this may be that accurately classifying lung
238 shadow is difficult since the large lung shadows of MACLD patients have a wide variety of
239 characteristics, and the fact that different characteristic patterns may sometimes coexist in a single
240 atypical shadow. In addition, excessive shadow classifications make evaluating shadows a
241 complex process and hamper the detection of statistically significant differences. Accordingly, as
242 a new method, we evaluated abnormal lung shadows with a major axis longer than 1 cm,
243 excluding spherical nodule shadows, as large shadows together. This approach resulted in large
244 shadows connected to bronchiectasis being commonly observed in MACLD but only rarely found
245 in PTB. We therefore believe that this method is a simple and useful approach to rule out a
246 diagnosis of PTB. Incidentally, it should be noted that the air bronchogram due to consolidation
247 is different from bronchiectasis.

248 In this study, there were no significant differences in the number or size of cavitary lesions,
249 but the thinnest part of the cavity wall in cases of MACLD was thinner than that in case of PTB.
250 This result is similar to several previous studies [6, 7]. Although these cavity findings may aid in

251 the differential diagnosis, caution should be practiced when ruling out PTB, because PTB with
252 cavitory lesions is thought to carry a high infection risk [20, 21].

253 Regarding the distribution of lung shadows, the present study showed that the frequency
254 of granular shadows in the RIL/LL was significantly higher with MACLD, while the frequency
255 of granular shadows and large shadows in the RUL/LUD was significantly higher with PTB [9,
256 12, 22]. It is considered that the RIL/LL bronchi anatomically diverge at an acute angle and are
257 oppressed by the anterior thoracic wall and heart with a low airway clearance, resulting in a
258 tendency for MAC bacteria fixation to occur [23]. PTB in adults often manifests as secondary
259 tuberculosis, and these lesions appear mainly in the pulmonary apex lesion and S6 of the lung
260 [24], possibly because pathogens hematogenously and lymphogenously migrating from the
261 primary infected lesion into the lung are fixed and proliferate in the apex area or S6 due to a low
262 ventilator perfusion ratio and relatively high oxygen concentration [25]. Bronchiectasis in PTB
263 cases seemed to show a tendency to appear in the RUL/LUD, which may indicate a site of
264 inflammation. Although various CT findings tended to co-exist in both MACLD and PTB cases,
265 the distribution (i.e., the segments or lobes in which granular shadows/large
266 shadows/bronchiectasis are present) is considered useful for the differential diagnosis.

267 Regarding other findings, pleural effusion was significantly more frequent in cases of PTB
268 than in MACLD. Furthermore, among PTB patients, pleural effusion was significantly more

269 frequent in immunodeficient cases than in normal-immune cases. The presence of pleural effusion
270 is rare with MACLD, so this lesion suggests a diagnosis of PTB, especially in immunodeficient
271 cases. According to previous reports, the thickness of the interlobular septa is typically greater
272 with PTB than with MACLD [9]. These differences in CT findings are considered due to PTB has
273 greater pathogenicity than MACLD, thereby causing more acute and stronger lymphatic
274 inflammation.

275 Several limitations associated with the present study warrant mention. First, the results
276 were based on a retrospective analysis of data from a single facility. Second, since MACLD
277 patients were diagnosed based on the identification of the pathogen through routine clinical
278 practice, there may have been a tendency to select severe cases. Third, the proportion of
279 immunodeficient patients differed between PTB cases and MACLD cases, which may have
280 affected the CT findings. To rule out the possibility of bias, a prospective study should be
281 conducted in the future.

282

283

284 **5. Conclusion**

285 Extensive bronchiectasis, cavity lesions with a thin wall, and granular/large shadows
286 connected to bronchiectasis were more frequently observed in cases of MACLD than in PTB.

287 Granular shadows, large shadows, and bronchiectasis were generally distributed to the RUL/LUD
288 in PTB cases. Therefore, chest CT findings would be useful for distinguishing PTB and MACLD
289 when typical findings are observed.

290

291 **Acknowledgments**

292 None.

293

294 **Conflicts of interest**

295 Yukari Tsubata received personal fees from AstraZeneca, Chugai Pharmaceutical and Daiichi-
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コメントの追加 [A1]: Collate acknowledgements in a separate section at the end of the article before the references and do not, therefore, include them on the title page, as a footnote to the title or otherwise. List here those individuals who provided help during the research (e.g., providing language help, writing assistance or proof reading the article, etc.).

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299 **References**

- 300 [1] Prevots DR, Marras TK. Epidemiology of human pulmonary infection with nontuberculous
301 mycobacteria: a review. Clin Chest Med 2015;36:13-34.
- 302 [2] Namkoong H, Kurashima A, Morimoto K, Hoshino Y, Hasegawa N, Ato M, et al.
303 Epidemiology of Pulmonary Nontuberculous Mycobacterial Disease, Japan. Emerg Infect
304 Dis 2016;22:1116-7.
- 305 [3] Morimoto K, Iwai K, Uchimura K, Okumura M, Yoshiyama T, Yoshimori K, et al. A steady
306 increase in nontuberculous mycobacteriosis mortality and estimated prevalence in Japan.
307 Ann Am Thorac Soc 2014;11:1-8.
- 308 [4] Tuberculosis Surveillance Center (2018). Tuberculosis in Japan - annual report 2018.
309 Department of Epidemiology and Clinical Research, the Research Institute of Tuberculosis:
310 Tokyo, Japan. https://jata.or.jp/english/dl/pdf/TB_in_Japan_2018.pdf. [Accessed 1 June
311 2019]
- 312 [5] Yuan MK, Chang CY, Tsai PH, Lee YM, Huang JW, Chang SC. Comparative chest computed
313 tomography findings of non-tuberculous mycobacterial lung diseases and pulmonary
314 tuberculosis in patients with acid fast bacilli smear-positive sputum. BMC Pulm Med
315 2014;14:65.
- 316 [6] Chu HQ, Li B, Zhao L, Huang DD, Zhang ZM, Xu JF, et al. Chest imaging comparison

317 between non-tuberculous and tuberculosis mycobacteria in sputum acid fast bacilli smear-
318 positive patients. *Eur Rev Med Pharmacol Sci* 2015;19:2429-39.

319 [7] Kim C, Park SH, Oh SY, Kim SS, Jo KW, Shim TS, et al. Comparison of chest CT findings
320 in nontuberculous mycobacterial diseases vs. *Mycobacterium tuberculosis* lung disease in
321 HIV-negative patients with cavities. *PLoS One* 2017;12:e0174240.

322 [8] Lynch DA, Simone PM, Fox MA, Bucher BL, Heinig MJ. CT features of pulmonary
323 *Mycobacterium avium* complex infection. *J Comput Assist Tomogr* 1995;19:353-60.

324 [9] Primack SL, Logan PM, Hartman TE, Lee KS, Müller NL. Pulmonary tuberculosis and
325 *Mycobacterium avium-intracellulare*: a comparison of CT findings. *Radiology*
326 1995;194:413-7.

327 [10] The Nontuberculous Mycobacteriosis Control Committee of the Japanese Society for
328 Tuberculosis and The Scientific Assembly for Infection and Tuberculosis of the Japanese
329 Respiratory Society. Guidelines for the diagnosis of pulmonary nontuberculous
330 mycobacterial disease-2008. *Kekkaku* 2011;86:37-9.

331 [11] Koh WJ, Lee KS, Kwon OJ, Jeong YJ, Kwak SH, Kim TS. Bilateral bronchiectasis and
332 bronchiolitis at thin-section CT: diagnostic implications in nontuberculous mycobacterial
333 pulmonary infection. *Radiology* 2005;235:282-8.

334 [12] Moore EH. Atypical mycobacterial infection in the lung: CT appearance. *Radiology*

335 1993;187:777-82.

336 [13] Obayashi Y, Fujita J, Suemitsu I, Kamei T, Nii M, Takahara J. Successive follow-up of chest
337 computed tomography in patients with Mycobacterium avium-intracellulare complex.
338 Respir Med 1999;93:11-5.

339 [14] Fujita J, Ohtsuki Y, Suemitsu I, Shigeto E, Yamadori I, Obayashi Y, et al. Pathological and
340 radiological changes in resected lung specimens in Mycobacterium avium intracellulare
341 complex disease. Eur Respir J 1999;13:535-40.

342 [15] Hatipoğlu ON, Osma E, Manisali M, Uçan ES, Balci P, Akkoçlu A, et al. High resolution
343 computed tomographic findings in pulmonary tuberculosis. Thorax 1996;51:397-402.

344 [16] Ko JM, Kim KJ, Park SH, Park HJ. Bronchiectasis in active tuberculosis. Acta Radiol
345 2013;54:412-7.

346 [17] Im JG, Itoh H, Shim YS, Lee JH, Ahn J, Han MC, et al. Pulmonary tuberculosis: CT findings-
347 -early active disease and sequential change with antituberculous therapy. Radiology
348 1993;186:653-60.

349 [18] Milliron B, Henry TS, Veeraraghavan S, Little BP. Bronchiectasis: Mechanisms and Imaging
350 Clues of Associated Common and Uncommon Diseases. Radiographics 2015;35:1011-30.

351 [19] Swensen SJ, Hartman TE, Williams DE. Computed tomographic diagnosis of
352 Mycobacterium avium-intracellulare complex in patients with bronchiectasis. Chest

353 1994;105:49-52.

354 [20] Matsuoka S, Uchiyama K, Shima H, Suzuki K, Shimura A, Sasaki Y, et al. Relationship
355 between CT findings of pulmonary tuberculosis and the number of acid-fast bacilli on
356 sputum smears. Clin Imaging 2004;28:119-23.

357 [21] Palaci M, Dietze R, Hadad DJ, Ribeiro FK, Peres RL, Vinhas SA, et al. Cavitory disease and
358 quantitative sputum bacillary load in cases of pulmonary tuberculosis. J Clin Microbiol
359 2007;45:4064-6.

360 [22] Ellis SM, Hansell DM. Imaging of Non-tuberculous (Atypical) Mycobacterial Pulmonary
361 Infection. Clin Radiol 2002;57:661-9.

362 [23] Reich JM, Johnson RE. Mycobacterium avium complex pulmonary disease presenting as an
363 isolated lingular or middle lobe pattern. The Lady Windermere syndrome. Chest
364 1992;101:1605-9.

365 [24] Krysl J, Korzeniewska-Kosela M, Müller NL, FitzGerald JM. Radiologic features of
366 pulmonary tuberculosis: an assessment of 188 cases. Can Assoc Radiol J 1994;45:101-7.

367 [25] Goodwin RA, Des Prez RM. Apical localization of pulmonary tuberculosis, chronic
368 pulmonary histoplasmosis, and progressive massive fibrosis of the lung. Chest 1983;83:801-
369 5.

370

371 **Figure caption**

372

373 Fig. 1 – Typical CT image. (A) Granular shadow: aggregation of small nodule shadows sized 1
374 cm or less (55-year-old female, MACLD). (B) Nodular shadow: spherical nodule shadow
375 exceeding 1 cm with a clear boundary (81-year-old female, MACLD). (C) Large shadow: ill-
376 defined massive shadow exceeding 1 cm (88-year-old male, PTB). (D) Bronchiectasis:
377 bronchiectasis noted on imaging and mucus stagnation in the lumen (73-year-old, MACLD). (E)
378 Cavitory lesion: a cavitory lesion with a thick wall (66-year-old male, PTB). (F) Tree-in-bud signs
379 (82-year-old, PTB). (G) Granular shadows connected to bronchiectasis (76-year-old female,
380 MACLD). (H) Large shadow connected to bronchiectasis (77-year-old female, MACLD). (I)
381 Schematic illustration ©. Granular shadow connected to bronchiectasis (black arrow). Large
382 shadow connected to bronchiectasis (white arrow).

383

384 Table 1 – Patient characteristics

	MACLD (n = 100)	PTB (n = 42)	p-value
Mean age ± standard deviation	71.5 ± 11.0	73.9 ± 16.8	0.400
Sex			
Male (%)	29 (29.0%)	30 (71.4%)	<0.001
Female (%)	71 (71.0%)	12 (28.6%)	
Immunocompromised* (%)	38 (38.0%)	28 (66.7%)	0.002

385 * Immunocompromised refers to poorly controlled diabetes, advanced renal impairment, liver failure,
 386 lymphocytopenia, taking immunosuppressive drugs, or receiving anti-cancer drug treatment.

387 MACLD, *Mycobacterium avium* complex lung disease; PTB, pulmonary tuberculosis.

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389

390 Table 2 – Comparison of chest CT findings

	MACLD (n = 100)	PTB (n = 42)	p-value
Granular shadow (≤1 cm)	95 (95.0%)	42 (100%)	0.168
Nodular shadow (>1 cm)	7 (7.0%)	7 (16.7%)	0.076
Large shadow (>1 cm)	67 (67.0%)	32 (76.2%)	0.277
Bronchiectasis	93 (93.0%)	18 (42.9%)	<0.001
Cavitary lesion	36 (36.0%)	11 (26.2%)	0.257
Tree-in-bud sign	68 (68.0%)	27 (64.3%)	0.668
Granular shadow connected to BE	81 (81.0%)	11 (26.2%)	<0.001
Large shadow connected to BE	56 (56.0%)	3 (7.1%)	<0.001
Calcification of the mediastinal/hilar lymph node	12 (12.0%)	18 (42.9%)	<0.001
Emphysema	19 (19.0%)	13 (31.0%)	0.120
Honeycomb lung	7 (7.0%)	2 (4.8%)	0.471
Pneumoconiosis	0 (0%)	2 (4.8%)	0.086
Pleural effusion	4 (4%)	16 (38.1%)	<0.001
Calcification inside the lung shadow	30 (30.0%)	26 (61.9%)	<0.001

391 CT, computed tomography; MACLD, *Mycobacterium avium* complex lung disease; PTB, pulmonary
 392 tuberculosis; BE, bronchiectasis.

393

394

395 Table 3 – Number of lobes with BE and number of cavity lesions

	MACLD	PTB	p-value
With BE	n = 93	n = 18	
Number of lobes with BE*	3.87±1.66	2.11±1.53	< 0.001
With cavitory lesions	n = 36	n = 11	
Number of lesions	3.06±3.26	2.73±1.49	0.749
Maximum lesion size (mm)	29.6±21.3	34.9±16.7	0.457
Maximum size of cavity wall (mm)	4.89±3.07	7.91±4.95	0.079
Minimum size of cavity wall (mm)	2.36±1.40	3.64±2.46	0.034

396 Data are presented as the mean±standard deviation.

397 * The number was counted dividing the left upper lobe into left upper division and lingula.

398 MACLD, *Mycobacterium avium* complex lung disease; PTB, pulmonary tuberculosis; BE, bronchiectasis.

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401 Table 4 – Distribution of granular shadows

	MACLD (n = 100)	PTB (n = 42)	p-value
RUL/LUD	78.0%	92.9%	0.034
RUL	69.0%	81.0%	0.145
LUD	52.0%	76.2%	0.007
Both RUL and LUD	43.0%	64.3%	0.021
RIL/LL	84.0%	61.9%	0.004
RIL	79.0%	52.4%	0.001
LL	65.0%	42.9%	0.015
Both RIL and LL	60.0%	33.3%	0.004
Segment 6	55.0%	59.5%	0.620
RS6	40.0%	47.6%	0.402
LS6	36.0%	40.5%	0.615
Both RS6 and LS6	21.0%	28.6%	0.330
Basilar Segment	72.0%	54.8%	0.046
RBS	58.0%	47.6%	0.257
LBS	57.0%	38.1%	0.040
Both RBS and LBS	43.0%	31.0%	0.180

402 MACLD, *Mycobacterium avium* complex lung disease; PTB, pulmonary tuberculosis; RUL, right upper
 403 lobe; LUD, left upper division; RIL, right intermediate lobe; LL, left lingula; RS6, right segment 6; LS6,
 404 left segment 6; RBS, right basilar segment; LBS, left basilar segment.

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 406

407 Table 5 – Distribution of large shadows

	MACLD (n = 100)	PTB (n = 42)	p-value
RUL/LUD	30.0%	64.3%	< 0.001
RUL	24.0%	45.2%	0.012
LUD	11.0%	23.8%	0.050
Both RUL and LUD	5.0%	4.8%	0.659
RIL/LL	51.0%	33.3%	0.054
RIL	37.0%	19.0%	0.036
LL	27.0%	14.3%	0.102
Both RIL and LL	13.0%	0%	0.008
Segment 6	16.0%	23.8%	0.272
RS6	10.0%	14.3%	0.319
LS6	9.0%	11.9%	0.400
Both RS6 and LS6	3.0%	2.4%	0.660
Basilar Segment	24.0%	33.3%	0.252
RBS	17.0%	19.0%	0.770
LBS	10.0%	19.0%	0.139
Both RBS and LBS	3.0%	4.8%	0.464

408 MACLD, *Mycobacterium avium* complex lung disease; PTB, pulmonary tuberculosis; RUL, right upper
 409 lobe; LUD, left upper division; RIL, right intermediate lobe; LL, left lingula; RS6, right segment 6; LS6,
 410 left segment 6; RBS, right basilar segment; LBS, left basilar segment.

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413 Table 6 – Distribution of bronchiectasis

	MACLD (n = 100)	PTB (n = 42)	p-value
RUL/LUD	76.0%	35.7%	< 0.001
RUL	74.0%	28.6%	< 0.001
LUD	48.0%	21.4%	0.003
Both RUL and LUD	46.0%	14.3%	< 0.001
RIL/LL	82.0%	14.3%	< 0.001
RIL	78.0%	11.9%	< 0.001
LL	62.0%	4.8%	< 0.001
Both RIL and LL	58.0%	2.4%	< 0.001
Segment 6	45.0%	11.9%	< 0.001
RS6	36.0%	9.5%	0.001
LS6	28.0%	4.8%	0.002
Both RS6 and LS6	19.0%	2.4%	0.009
Basilar Segment	52.0%	9.5%	< 0.001
RBS	50.0%	7.1%	< 0.001
LBS	31.0%	7.1%	0.002
Both RBS and LBS	29.0%	4.8%	0.001

414 MACLD, *Mycobacterium avium* complex lung disease; PTB, pulmonary tuberculosis; RUL, right upper
 415 lobe; LUD, left upper division; RIL, right intermediate lobe; LL, left lingula; RS6, right segment 6; LS6,
 416 left segment 6; RBS, right basilar segment; LBS, left basilar segment.

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419 Table 7 – Distribution of cavitory lesions

	MACLD (n=100)	PTB (n=42)	p-value
RUL/LUD	23.0%	21.4%	0.838
RUL	19.0%	11.9%	0.303
LUD	6.0%	11.9%	0.193
Both RUL and LUD	2.0%	2.4%	0.654
RIL/LL	14.0%	0%	0.006
RIL	9.0%	0%	0.038
LL	7.0%	0%	0.081
Both RIL and LL	2%	0%	0.494
Segment 6	7.0%	14.3%	0.146
RS6	6.0%	7.1%	0.529
LS6	4.0%	7.1%	0.341
Both RS6 and LS6	3.0%	0%	0.346
Basilar Segment	10.0%	9.5%	0.600
RBS	9.0%	7.1%	0.503
LBS	4.0%	2.4%	0.536
Both RBS and LBS	3.0%	0%	0.346

420 MACLD, *Mycobacterium avium* complex lung disease; PTB, pulmonary tuberculosis; RUL, right upper
421 lobe; LUD, left upper division; RIL, right intermediate lobe; LL, left lingula; RS6, right segment 6; LS6,
422 left segment 6; RBS, right basilar segment; LBS, left basilar segment.

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